MODIFIED PROTEASES THAT INHIBIT COMPLEMENT ACTIVATION

RELATED APPLICATIONS

Benefit of priority is claimed to U.S. provisional application Serial No. 60/729,817, filed October 21, 2005, entitled "MODIFIED PROTEASES THAT INHIBIT COMPLEMENT ACTIVATION," to Edwin Madison. Where permitted, the subject matter of this application is incorporated by reference in it entirety.

This application is related to U.S. Patent Application Serial No. (Attorney Docket No. 19049-003001/4903), filed October 20, 2006, entitled "MODIFIED PROTEASES THAT INHIBIT COMPLEMENT ACTIVATION," to Edwin Madison, Jack Nguyen, Sandra Waugh Ruggles and Christopher Thanos, which also claims priority to U.S. Provisional Application Serial No. 60/729,817.

This application is related to U.S. application Serial No. 10/677,977, filed October 02, 2003, entitled *Methods of Generating and Screening for Proteases with Altered Specificity*; to U.S. application Serial No. 11/104,110, filed April 12, 2005, entitled *Cleavage of VEGF and VEGF Receptor by Wild-Type and Mutant MTSP-1*; and to U.S. application Serial No. 11/104,111, filed April 12, 2005, entitled *Cleavage of VEGF and VEGF Receptor by Wild-Type and Mutant Protease*.

Where permitted, the subject matter of each of the above-noted applications is incorporated by reference in its entirety.

FIELD OF INVENTION

Provided are methods for and compounds for modulating the complement system. In particular, compounds are provided that inhibit complement activation and compounds are provided that promote complement activation. The compounds are therapeutics by virtue of their effects on the complement system. Hence, the compounds that inhibit complement activation can be used for treatment of ischemic and reperfusion disorders, including myocardial infarction and stroke, sepsis, autoimmune diseases, inflammatory diseases and diseases with an inflammatory component, including Alzheimer's Disease and other neurodegenerative disorders.

BACKGROUND

The complement (C) system is part of the immune system and plays a role in eliminating invading pathogens and in initiating the inflammatory response. The

complement system of humans and other mammals involves more than 30 soluble and membrane-bound proteins that participate in an orderly sequence of reactions resulting in complement activation. The blood complement system has a wide array of functions associated with a broad spectrum of host defense mechanisms including anti-microbial and anti-viral actions. Products derived from the activation of C components include the non-self recognition molecules C3b, C4b and C5b, as well as the anaphylatoxins C3a, C4a and C5a that influence a variety of cellular immune responses. These anaphylatoxins also act as pro-inflammatory agents.

The complement system is composed of an array of enzymes and non-enzymatic proteins and receptors. Complement activation occurs by one of three primary modes known as the "classical" pathway, the "alternative" pathway and the "lectin" pathway (see FIGURE 1). These pathways can be distinguished by the process that initiates complement activation. The classical pathway is initiated by antibody-antigen complexes or aggregated forms of immunoglobulins; the alternative pathway is initiated by the recognition of structures on microbial and cell surfaces; and the lectin pathway, which is an antibody-independent pathway, is initiated by the binding of mannan binding lectin (MBL, also designated mannose binding protein) to carbohydrates such as those that are displayed on the surface of bacteria or viruses. Activation of the cascades results in production of complexes involved in proteolysis or cell lysis and peptides involved in opsonization, anaphylaxis and chemotaxis.

The complement cascade, which is a central component of an animal's immune response, is an irreversible cascade. Numerous protein cofactors regulate the process. Inappropriate regulation, typically inappropriate activation, of the process is a facet of or can occur in a variety of disorders that involve inappropriate inflammatory responses, such as those observed in acute and chronic inflammatory diseases. These diseases and disorders include autoimmune diseases, such as rheumatoid arthritis and lupus, cardiac disorders and other inflammatory diseases, such as sepsis and ischemia-reperfusion injury.

Because of the involvement of the complement pathways in a variety of diseases and conditions, components of the complement pathways are targets for therapeutic intervention, particularly for inhibition of the pathway. Examples of such

therapeutics include synthetic and natural small molecule therapeutics, antibody inhibitors, and recombinant soluble forms of membrane complement regulators. There are limitations to strategies for preparing such therapeutics. Small molecules have short half-lives *in vivo* and need to be continually infused to maintain complement inhibition thereby limiting their role, especially in chronic diseases. Therapeutic antibodies result in an immune response in a subject, and thus can lead to complications in treatment, particularly treatments designed to modulate immune responses. Thus, there exists an unmet need for therapeutics for treatment of complement-mediated diseases and diseases in which complement activation plays a role. These include acute and chronic inflammatory diseases. Accordingly, among the objects herein, it is an object to provide such therapeutics to target the activation of the complement cascade and to provide therapeutics and methods of treatment of diseases.

SUMMARY

Provided herein are therapeutics and methods that target the activation of the complement cascade and methods of treatment of diseases, including acute and chronic inflammatory diseases. The therapeutics are non-complement proteases that target complement pathway substrates. Included among the non-complement proteases are unmodified proteases that cleave their native substrate as well as a complement substrate and also proteases modified to have increased selectivity or substrate specificity for a target substrate. The modified proteases can exhibit reduced or altered activity with respect to their native substrates.

Among the methods provided herein are methods of modulating complement activation by contacting a non-complement protease with any one or more, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30 or more target substrates of a complement pathway, whereby a target substrate protein is cleaved such that complement activation in a pathway comprising the target substrate is altered. Uses of proteases for treatment and/or for formulation of medicaments also are provided. Target substrates for these methods and for any of the methods and uses provide herein are complement proteins, including: C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a,

C2b, C2a, C3b, C3a, Ba, Bb and ficolin. Contacting can be effected *ex vivo*, *in vitro* and/or *in vivo*. Exemplary targets include any of those having a sequence of amino acids set forth in any of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, 344, 660-662 and a fragment of any of the targets that exhibits a complement pathway activity, or allelic or species variants thereof or polypeptides having 60, 70, 80, 85, 90, 95, 96, 97, 98, 99% or more sequence identity.

For all and for any methods and uses provided herein, the target substrates can be present in a body fluid or tissue sample, or can be a collection of target substrates or any other composition containing such substrates. Depending upon the target substrate(s), complement activation can be inhibited or activated. The methods target one or more any complement pathway. Thus, the complement pathway modulated can be selected from among one or more of the classical, alternative and lectin pathways of complement. The non-complement proteases contain modifications at any one or more amino acid residues, such as 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 20, 25, 30, 35 or more residues, compared to an unmodified or scaffold protease. The modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate. Exemplary unmodified or scaffold proteases include any one of a serine protease, a cysteine protease, an aspartic protease, a threonine protease and a metallo-protease, such as, for example, granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof. For example, the scaffold protease comprises a sequence of amino acids set forth in any one of SEQ ID NOS: 2, 4, 8, 77, 79, 83, 85, 87, 89, 93, 99, 117, 119, 121, 123, 132, 134, 138, 142, 144, 146, 148, 162, 166, 168, 170, 172, 174, 176, 178, 180, 182, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 218, 220, 222, 224, 226, 238, 248, 250, 260, 262, 280, 282, 373, 375, 377, 379, 381, 383, 385, 387, 547, 549, and 551 and catalytically active portions thereof, allelic and

species variants thereof and polypeptides having 60, 70, 80, 85, 90, 95, 96, 97, 98, 99% or more sequence identity. MT-SP1 or a fragment thereof, such as the polypeptide sequence set forth in SEQ ID NO: 2 and 10, respectively, is exemplary of a scaffold protease. C2 or C3 proteins of a complement pathway(s) are exemplary target substrates of an MT-SP1 protease, modified MT-SP1 protease, or catalytically active portions thereof.

Modification of an MT-SP1 protease or a catalytically active portion thereof include modification(s) at positions 146, 224, 41, and/or 151, based on chymotrypsin numbering. Such modified MT-SP1 proteases include those with any of the following modifications: I41T/Y146D/G151L/K224F, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, AND I41T/Y146D/G151L/Q175D/K224N, I41T/Y146D/G151L/K224N, Y146D/G151L/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering. In particular, a modified MT-SP1 contains amino acid modifications I41T/Y146D/G151L/K224F.

The modifications can be in any one or more amino acids that contribute to extended substrate specificity or secondary sites of interaction, such as, for example, modifications in an MT-SP1 protease or a catalytically active portion thereof that correspond to any one or more of amino acid positions 97, 146, 192, and 224 of an MT-SP1 protease, based on chymotrypsin numbering. Exemplary of such modifications are one or more of F97, Y146, Q192, and K224 of the MT-SP1 protease, based on chymotrypsin numbering, such as F97D, F97E, F97A, F97W, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Q192R, Q192V, K224A, and K224F. Exemplary of such modified MT-SP1 proteases including those polypeptides having a sequence of amino acids set forth in any of SEQ ID NOS: 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 14, 38, and 40 and 405-418. Other examples of a modified MT-SP1 protease or a catalytically active portion thereof include amino acid

modifications Y146D/K224F or Y146E, such as those corresponding to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in SEQ ID NOS:12, 404, 28 or 412.

MT-SP1 protease and catalytically active portion thereof include polypeptides that contain one or more of the following modifications: F97N, F97D, F97E, F99Y, F99V, F99W, D217A, D217V, F97A, F97W, F99A, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, W215F, W215Y, Q192V, Q192R, Q192F, K224A, K224F, M180E, Y146D/K224F, D96A, Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, I41T/Y146E/Q175D/K224L, I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F,

I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering. Exemplary of such modified MT-SP1 proteases, or catalytically active portions thereof, include those polypeptides having a sequence of amino acids set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710. In particular, a modified MT-SP1 protease, or a catalytically active portion thereof, is one having a sequence of amino acids set forth in SEQ ID NOS: 596 or 650.

For all methods and uses provided herein, the modification can be selected such that the modified protease, such as MT-SP1, cleaves a substrate recognition site of the target substrate. Target substrate are any of the complement pathway polypeptides noted above and known to those of skill in the art, including for example, C2 and/or C3. For example, where the target substrate is C2 the substrate recognition site includes a sequence of amino acids of SLGR (SEQ ID NO:392).

Other recognition sites targeted in the methods and uses provided herein include a Factor I substrate recognition site, such as LPSR (SEQ ID NO:388), SLLR (SEQ ID NO:389), or HRGR (SEQ ID NO: 390). Modifications in the MT-SP1 protease or a catalytically active portion can correspond to any one or more of amino acid positions 174, 217, 96, 192, 146, or 99 of an MT-SP1 protease, based on chymotrypsin numbering., such as any one or more of amino acids Q174, D217, D96, Q192, Y146, and F99 of a MT-SP1 protease, based on chymotrypsin numbering. Exemplary of such modifications are modifications selected from among one ore more of: Q174H, D217Q, D217N, D217H, D96A, D96V, D96F, D96S, D96T, Q192L, Q192I, Q192F, Y146F, F99A, F99V, F99S, and F99G (see, *e.g.*, the polypeptides having a sequence of amino acids set forth in any of SEQ ID NOS: 41-57 or 419-435.

Another recognition site includes the sequence of amino acids LPSR. Exemplary of a modified protease modified for recognition thereof are: an MT-SP1 protease or a catalytically active portion thereof having modifications at sites corresponding to any one or more of amino acid positions 174, 180, 215, 192, or 99 of

an MT-SP1 protease, based on chymotrypsin numbering, such as, for example, any one or more of amino acids Q174, M180, W215, Q192, or F99 of a MT-SP1 protease, based on chymotrypsin numbering. Exemplary of such modifications is any one or more of Q174F, Q174V, Q174L, Q174Y, M180E, W215F, W215Y, Q192K, Q192R, Q192Y, and F99Y (see, *e.g.*, modified MT-SP1 polypeptides having a sequence of amino acids as set forth in any of SEQ ID NOS: 36, 58, 59, 61, 62, 69, 416, 436, 437, 439, 440, 447, or 524-533).

Another substrate recognition site for use in the methods herein includes the sequence of amino acids HRGR. Exemplary of a protease with modifications to recognize such sites are an MT-SP1 protease or a catalytically active portion thereof that has modifications that correspond(s) to modifications at any one or more of amino acid positions 215, 174, 217, 192 and 99 of an MT-SP1 protease, based on chymotrypsin numbering, such as, for example, W215, Q174, D217, Q192 and F99 of an MT-SP1 protease, based on chymotrypsin numbering. Examplary thereof are modification selected from among: any one or more of W215F, W215Y, Q174A, Q174V, Q174 F, Q174R, Q174K, D217A, D217V, Q192E, F99W and F99Y (*e.g.*, an MT-SP1 protease or a catalytically active portion thereof corresponding to a modified MT-SP1 polypeptide containing a sequence of amino acids as set forth in any of SEQ ID NOS: 58-69 and 436-447.

Methods for treatment of complement-mediated disorders and disorders whose symptoms are ameliorated by modulating a complement pathway, including one or more of the classical, alternative and lectin pathways, are provided. In practicing the methods, one ore more non-complement proteases is/are contacted with one ore more target substrates, such as by administration *in vitro*, *in vivo* or *ex vivo*, whereby the non-complement protease cleaves any one or more target substrates of a complement pathway such that complement activation in a pathway comprising the target substrate is altered. Uses of the non-complement proteases for treatment of such diseases and disorders and/or for formulation of medicaments for such treatment also are provided. Modulation includes inhibition or enhancement (increasing) complement activation. Inhibition of complement activation can lead to a reduction in inflammatory symptoms associated with a complement-mediated disorder.

Exemplary of inflammatory disorders are neurodegenerative disorders and cardiovascular disorders, such as, but are not limited to, sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), Ischemia-reperfusion injury and Guillan-Barre syndrome. Complement-mediated disorders can result from a treatment of a subject. Ischemia-reperfusion injury can be caused by an event or treatment selected from among myocardial infarct (MI), stroke, angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.

The methods of treatment provided herein can be effected by administering to a subject a non-complement protease effected prior to treatment of the subject for the manifested disorder. As noted administering can be effected by contacting a body fluid or tissue sample *in vitro*, *ex vivo*, or *in vivo* with a non-complement protease. Complement-mediated ischemia-reperfusion injury is exemplary of such disorders. The treatment causing such disorder is angioplasty or coronary artery bypass graft.

As noted above, in any of the methods and uses provide herein, target substrates include one or more of C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a, C2b, C2a, C3b, C3a, Ba , Bb and ficolin, such as a substrate that contains a sequence of amino acids set forth in any one of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, or 344, or is fragment thereof that exhibits a complement activity.

In these methods and uses and all methods and uses provided herein, the non-complement protease can include modifications at any one or more amino acid residues compared to an unmodified or scaffold protease, wherein the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate. Unmodified or scaffold protease include any one of a serine protease, cysteine protease, aspartic protease, threonine protease, or metallo-protease, such as granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-

plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof. Exemplary are those that contain or have a sequence of amino acids as set forth in any one of SEQ ID NOS: 2, 4, 8, 77, 79, 83, 85, 87, 89, 93, 99, 117, 119, 121, 123, 132, 134, 138, 142, 144, 146, 148, 162, 166, 168, 170, 172, 174, 176, 178, 180, 182, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 218, 220, 222, 224, 226, 238, 248, 250, 260, 262, 280, 282, 373, 375, 377, 379, 381, 383, 385, 387, 547, 549, and 551 and catalytically active portions thereof. MT-SP1 is an exemplary scaffold protease provided herein and is as described above. Cleavage can be targeted to the recognition sequences as described above. Any modified MT-SP1 described herein can be used in the methods of treatment including such as any MT-SP1 described above. Exemplary of modified MT-SP1 polypeptides or catalytically active portions thereof for use in the treatment provided herein include any having a sequence of amino acids set forth in any of 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710. In particular, an MT-SP1 polypeptide or catalytically active portion thereof for use in the treatments provided herein has a sequence of amino acids set forth in SEQ ID NOS:596 or 650.

In any or all of the methods and uses provided herein, a non-complement protease or a catalytically active portion thereof can be administered in combination with a second agent or treatment for treating a complement-mediated disorder or any other disorder. The second agent or treatment can be administered simultaneously, sequentially or intermittently with the non-complement protease. The second agent can be administered as a separate composition or in the same composition as the non-complement protease. Exemplary of second agents are anti-inflammatory agent and anticoagulants, such as, but not limited to, any one or more of an NSAID, antimetabolite, corticosteroid, analgesic, cytotoxic agent, pro-inflammatory cytokine inhibitor, anti-inflammatory cytokines, B cell targeting agents, compounds targeting T antigens, adhesion molecule blockers, chemokines receptor antagonists, kinase inhibitors, PPAR-γ ligands, complement inhibitors, heparin, warfarin, acenocoumarol,

phenindione, EDTA, citrate, oxalate, argatroban, lepirudin, bivalirudin, and ximelagatran.

Also provided are combinations of the non-complement proteases and other elements, such as reagents, second agents, and devices and containers for administering the proteases and/o agents and any other elements. The combinations can be for practicing or effecting the methods and uses provided herein. Hence provided, for example, are combinations of elements that include: (a) a non-complement protease that cleaves any one or more complement target substrates of a complement pathway such that complement activation in a pathway comprising the target substrate is altered; and (b) a second agent or agents for treating a complement-mediated disorder, such as, but not limited to anti-inflammatory agent(s) or anticoagulant(s), such as, for example, any one or more of a NSAID, antimetabolite, corticosteroid, analgesic, cytotoxic agent, pro-inflammatory cytokine inhibitor, anti-inflammatory cytokines, B cell targeting agents, compounds targeting T antigens, adhesion molecule blockers, chemokines receptor antagonists, kinase inhibitors, PPAR-γ ligands, complement inhibitors, heparin, warfarin, acenocoumarol, phenindione, EDTA, citrate, oxalate, argatroban, lepirudin, bivalirudin, and ximelagatran.

As noted, the combinations are for practicing or effecting any of the methods herein for modulating a complement pathway, such as one or more of the classical, alternative, or lectin pathways of complement. Target substrates and scaffold proteases include any of those set forth above. For example, scaffold proteases include any set forth Table 14, and allelic variations, isoforms and catalytically active portions of the proteases set forth in Table 14. Exemplary of such proteases, include any that has or contains a sequence of amino acids set forth in any one of SEQ ID NOS: 2, 4, 8, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 269, 270, 272,

274, 276, 278, 280, 282, 284, 286, 287, 289, 291, 293, 295, 297, 373, 375, 377, 379, 381, 383, 385, 387, 544, 545, 547, 549, and 551, or a catalytically active portion thereof or an allelic or species variant thereof. In some examples, the protease used in the combinations is an MT-SP1 or catalytically active portion thereof, such as an MT-SP1 set forth in SEQ ID NO: 2 or 10, and the variants noted above. As noted above, MT-SP1 protease and catalytically active portion thereof include polypeptides that contain one or more of the following modifications: F97N, F97D, F97E, F99Y, F99V, F99W, D217A, D217V, F97A, F97W, F99A, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, W215F, W215Y, Q192V, Q192R, Q192F, K224A, K224F, M180E, Y146D/K224F, D96A, Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, I41T/Y146E/Q175D/K224L, I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N,

Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering. Exemplary of such modified MT-SP1 proteases, or catalytically active portions thereof, include those polypeptides having a sequence of amino acids set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710. In particular, a modified MT-SP1 protease, or a catalytically active portion thereof, is one having a sequence of amino acids set forth in SEQ ID NOS: 596 or 650. In some cases, the modifications in an MT-SP1 protease or a catalytically active portion thereof include modifications of any one or more amino acids that contribute to extended substrate specificity or secondary sites of interaction. Exemplary of this include, but are not limited to, any that correspond to any one or more of amino acid positions 97, 146, 192, and 224 of an MT-SP1 protease, based on chymotrypsin numbering. Exemplary of such modifications are modifications in any one or more of amino acids F97, Y146, Q192, and K224 of the MT-SP1 protease, based on chymotrypsin numbering, such as modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from any one or more of F97D, F97E, F97A, F97W, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Q192R, Q192V, K224A, and K224F (*e.g.*, an MT-SP1 protease or a catalytically active portion thereof corresponds to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in any of SEQ ID NOS: 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 14, 38, and 40 and 405-418 and/or in an MT-SP1 protease or a catalytically active portion thereof with modifications at positions Y146D and K224F or Y146E, such as those modified MT-SP1 polypeptides having a sequence of amino acids as set forth in SEQ ID NO:12, 404, 28 or 412).

In the combinations and methods and uses provided herein, the non-complement protease can cleave a substrate recognition site of the target substrate. Exemplary recognition sites are set forth above.

Also provided are particular modified non-complement proteases. For example provided are non-complement proteases containing modifications in any one or more amino acids of a scaffold protease, where the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate, where the target substrate is a complement protein, such as any target substrate and mixture thereof and source thereof set forth above. The modified non-complement protease includes any suitable scaffold including any noted above, such as a scaffold protease selected from among granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof. Target substrates include any set forth above, such as, but not limited to C2 and/or C3.

Exemplary modified non-complement proteases include those based on an MT-SP1 scaffold (full-length or a catalytically active portion thereof). The MT-SP1 scaffold can include one, or at least two or more modifications, where one modification is at position 146 and the second modification is at position 224, based on chymotrypsin numbering, provided that:

(i) where the protease includes only two modifications, the protease does not include Y146D and K224F as the two modification; and (ii) where the protease contains three modifications, the protease does not include F99V or I or L or T with Y146D and K224F. For example, such modified non-complement protease can one containing at least two or more modifications, where one modification is a position 146 and the second is at position 224, based on chymotrypsin numbering, provided that: (i) where the protease includes only two modifications, the protease does not include Y146D and K224F as the two modification; and (ii) where the protease contains three modifications, the protease does not include F99V or I or L or T with Y146D and K224F. An MT-SP1 protease, or catalytically portion thereof, also includes a modified protein containing one, or at least two or more modifications at position 141

and/or position 41. Exemplary of any of the above modified MT-SP1 proteases or catalytically active portions thereof include a modified MT-SP1 containing modifications of any of I41T/Y146D/G151L/K224F, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, AND I41T/Y146D/G151L/Q175D/K224N, I41T/Y146D/G151L/K224N, Y146D/G151L/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N based on chymotrypsin numbering.

Exemplary of such modified protease include an MT-SP1 protease or a catalytically active portion thereof selected from any one or more of D96A, D96V, D96F, D96F, D96S, D96T, F99S, F99G, Q174H, Q174A, Q174V, Q174F, Q174R, Q174K, Q174L, Q174Y, Q192L, Q192I, Q192E, Q192K, Q192Y, D217Q, D217N, D217H, K224A, based on chymotrypsin numbering. Exemplary are MT-SP1 proteases that contain or have a sequence of amino acids as set forth in any one of SEQ ID NOS: 41-51, 56, 57, 60-64, 67, 419-429, 431, 434, 435, 438-442, or 445.

Exemplary modified MT-SP1 proteases, or catalytically active portion thereof, also include any having any of the following modifications: Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T,

I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, and I41T/Y146E/Q175D/K224L, , I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering. Exemplary of such proteases are any having a sequence of amino acids set forth in any of SEQ ID NOS: 41-51, 56, 57, 60-64, 67, 69, 419-429, 431, 434, 435, 438-442, 445, 524, 525, 527-530, 532, 533, 552-659, or 663-710. In particular, a modified MT-SP1 protease or catalytically active portion thereof has a sequence of amino acids set forth in SEQ ID NOS: 596 or 650. Included among the modified MT-SP1 proteases, or catalytically active portions thereof, provided herein are those that cleave a target substrate, typically, at a substrate recognition site in the target substrate. Exemplary of target substrates include C2 or C3. Cleavage of C2 can be at a substrate recognition site SLGR (SEQ ID NO:392) in C2.

Among the modified non-complement protease that contain modifications in any one or more amino acids of a scaffold protease, where the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate, wherein the target substrate is a complement protein that are provided are such modified non-complement protease that not cleave a VEGF or VEGFR or that exhibit a reduction in any cleavage activity of a VEGF or VEGFR or that exhibit greater substrate specificity or activity for a target substrate such as a

complement protein, than for VEGF or VEGFR with the modification compared to without the modification. For example, the non-complement protease cleaves a complement protein with at least or about 1-fold, 1.5-fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, 200-fold, 500-fold, 1000-fold, or more greater specificity or activity than it cleaves VEGF or VEGFR. The target substrates include complement proteins, such as, but not limited to any one or more of C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a, C2b, C2a, C3b, C3a, Ba, Bb and ficolin. Exemplary target substrates include, but are not limited to target substrates containing a sequence of amino acids set forth in any one of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340 and 344 or a fragment thereof that exhibits a complement activity.

Scaffold proteases include any protease, including, a serine protease, cysteine protease, aspartic protease, threonine protease, or metallo-protease, such as any set forth in Table 14, and allelic and species variants thereof, isoforms and catalytically active portions, and modified forms thereof that have 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98, 99% or more sequence identity to any provided in the Table or elsewhere herein, such as a scaffold protease that contains a sequence of amino acids as set forth in any one of SEQ ID NOS: 2, 4, 8, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 269, 270, 272, 274, 276, 278, 280, 282, 284, 286, 287, 289, 291, 293, 295, 297, 373, 375, 377, 379, 381, 383, 385, 387, 544, 545, 547, 549, and 551, and catalytically active portions thereof. The scaffolds can be used for preparing modified proteases and in any method or use herein. As discussed above, MT-SP1 or a catalytically active fragment thereof is exemplary of such proteases. An exemplary MT-SP1 protease or portion thereof has the sequence of amino acids set forth in SEQ ID NO: 2 or 10. Modification include any that alter substrate specificity or

selectivity, particularly those that increase substrate specificity or selectivity for a complement protein. Exemplary of such modifications are MT-SP1 proteases or a catalytically active portions thereof with any of the following modifications D96A, D96V, D96F, D96F, D96S, D96T, F97D, F97E, F97A, F97W, F99A, F99S, F99G, F99W, F99Y, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Q174H, Q174A, Q174V, Q174F, Q174R, Q174K, Q174L, Q174Y, M180E, Q192R, Q192V, Q192L, Q192I, Q192F, Q192E, Q192K, Q192Y, W215F, W215Y, D217Q, D217N, D217H, D217A, D217V, K224A, Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, and I41T/Y146E/Q175D/K224L, , I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F,

I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering.

and allelic and species variants and isoforms thereof and variants with 60, 65, 70, 75, 80, 85, 90, 95, 96, 97, 98, 99% or more sequence identity therewith and including the corresponding modification. For example, modified MT-SP1 polypeptide containing a sequence of amino acids as set forth in any of SEQ ID NOS: 41-51, 56, 57, 60-64, 67, 69, 419-429, 431, 434, 435, 438-442, 445, 524, 525, 527-530, 532, 533, 552-659, or 663-710.

Also provided are pharmaceutical compositions containing any of the modified non-complement proteases or elements of the combinations provided herein. The pharmaceutical compositions include, as needed, pharmaceutically acceptable excipients and other components. The compositions are formulated for any desired or suitable route of administration, including, but not limited to systemic, oral, nasal, pulmonary, local, or topical administration.

Kits are provided. The kits can be used in practicing the methods. Kits containing the combinations are provided. Kits containing the pharmaceutical compositions also are provided. The kits also can contain devices for administration of the composition and/or proteases and, optionally, instructions for administration and other reagents and products employed in the methods.

Also provided are nucleic acid molecules that encode any of the modified non-complement proteases. Included among these are nucleic acid molecules that encode or that hybridize under medium or high stringency to any nucleic acid that encodes any of the polypeptides set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710. Also included among the nucleic acid molecules are those selected from among:

a) a nucleic acid molecule comprising a sequence of nucleotides set forth in any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 451-455, 457-462, 464-479, and 534-538;

b) a nucleic acid molecule comprising at least 60, 65, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 % sequence identity to any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 451-455, 457-462, 464-479, 534-538;

c) a nucleic acid that hybridizes under conditions of medium or high stringency along at least 70% of its full length to a nucleic acid molecule comprising a sequence of nucleotides set forth in any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 451-455, 457-462, 464-479, 534-538;

d) a nucleic acid molecule that comprises degenerate codons of a), b), or c); or

e) a nucleic acid molecule comprising splice variants or allelic variants of any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 451-455, 457-462, 464-479, 534-538 or any of a)-d), or .

nucleic acid molecule is selected from among:

a) a nucleic acid molecule comprising a sequence of nucleotides set forth in any of SEQ ID NOS: 480-493, 495-499, 501-506, 508-523, 539-543;

b) a nucleic acid molecule comprising at least 60, 65, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 % sequence identity to any of SEQ ID NOS: 480-493, 495-499, 501-506, 508-523, 539-543;

c) a nucleic acid that hybridizes under conditions of medium or high stringency along at least 70% of its full length to a nucleic acid molecule comprising a sequence of nucleotides set forth in any of SEQ ID NOS: 480-493, 495-499, 501-506, 508-523, 539-543;

d) a nucleic acid molecule that comprises degenerate codons of a), b), or c); or

e) a nucleic acid molecule comprising splice variants or allelic variants of any of SEQ ID NOS: 480-493, 495-499, 501-506, 508-523, 539-543 or any of a)- d).

Vectors containing the nucleic acid molecules. Vectors include eukaryotic and prokaryotic expression vectors, including mammalian and yeast vectors. Cells containing the nucleic acid molecules and/or vectors also are provided. Exemplary expression vector include but are not limited to: an adenovirus vector, an adeno-associated virus vector, EBV, SV40, cytomegalovirus vector, vaccinia virus vector,

herpesvirus vector, a retrovirus vector, a lentivirus vector and an artificial chromosome. Methods for production or preparation of the encoded non-complement proteases are provided. The vectors or nucleic acid molecules are introduced into cells and cultured under conditions, whereby the protease is expressed. The nucleic acid molecule can include sequence encoded a signal sequence to direct trafficking of the expressed protease, such as a signal sequence for secretion. The expressed proteases can be purified by routine methods known to those of skill in the art.

Methods of treatment by administering to a subject a nucleic acid molecule, vector or cell are provided. The diseases treated include any mediated by or involving a complement protein or the complement pathway, such as diseases with an underlying inflammatory component or pathology. Vectors include an expression vector that integrated into a host cell's chromosome or a vector that remains episomal.. Administration can be *in vivo* or *ex vivo*. Ex *vivo* treatment includes administering the nucleic acid into a cell *in vitro,* followed by administration of the cell into the subject. The cell can be from a suitable (compatible) donor or from the subject, such as a human, to be treated.

Also provided are fusion proteins containing a catalytically active portion of any of the non-complement proteases that is fused to a non-protease polypeptide. Fusion can be by insertion into the non-protease polypeptide or linkage at either end.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 depicts an overview of the classical, lectin, and alternative complement pathways and the activation of the terminal complement complex, the membrane attack complex (MAC). In particular, the figure depicts many of the more than 30 proteins that participate in the complement cascade, their action within the cascade, and where applicable, their points of convergence among the complement pathways. For example, the three pathways converge upon the generation of a C3 convertase, which cleaves C3 to form a C5 convertase yielding the formation of the MAC complex. The figure also depicts the generation of many of the complement cleavage products. All proteins depicted in the pathways can serve as substrate targets.

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A. Definitions

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the invention(s) belong. All patents, patent applications, published applications and publications, Genbank sequences, databases, websites and other published materials referred to throughout the entire disclosure herein, unless noted otherwise, are incorporated by reference in their entirety. In the event that there are a plurality of definitions for terms herein, those in this section prevail. Where reference is made to a URL or other such identifier or address, it understood that such identifiers can change and particular information on the internet can come and go, but equivalent information can be found by searching the internet. Reference thereto evidences the availability and public dissemination of such information.

As used herein, MBL (mannose binding lectin) also is designated mannose-binding protein (MBP).

As used herein, complement activation refers to the sequential activation of serum components C1 through C9, initiated by a variety of activators including, for example, antigen-antibody complex, lipopolysaccharide, or microbial polysaccharides, and producing an inflammatory response via any pathway.

As used herein, a "complement protein" or a "complement component" is a protein of the complement system that functions in the host defense against infections and in the inflammatory process. Complement proteins constitute target substrates for the proteases and modified proteases provided herein.

Complement proteins are a group of interacting blood proteins and glycoproteins found in all vertebrates. There are at least 30 soluble plasma proteins in addition to cell surface receptors that bind complement reaction products and that occur on inflammatory cells and cells of the immune system. In addition, there are regulatory membrane proteins that protect host cells from accidental complement attack. Complement proteins include those that function in the classical pathway, for example, C2, those that function in the alternative pathway, for example, Factor B, and those that function in the lectin pathway, for example MASP-1. Among the complement proteins are proteases that participate in the complement pathways. In addition, as used herein, complement proteins include any of the "cleavage products" (also referred to as "fragments") that are formed upon activation of the complement cascade. Also included among complement proteins are inactive or altered forms of complement proteins, such as iC3 and C3a-desArg.

Thus, complement proteins include, but are not limited to: C1q, C1r, C1s, C2, C3, C3a, C3b, C3c, C3dg, C3g, C3d, C3f, iC3, C3a-desArg, C4, C4a, C4b, iC4, C4a-desArg, C5, C5a, C5a-des-Arg, C6, C7, C8, C9, MASP-1, MASP-2, MBL, Factor B, Factor D, Factor H, Factor I, CR1, CR2, CR3, CR4, properdin, C1Inh, C4bp, MCP, DAF, CD59 (MIRL), clusterin and HRF and allelic and species variants of any complement protein.

As used herein, a "native" form of a complement protein is one which can be isolated from an organism such as a vertebrate in the absence of complement activation, and which has not been intentionally modified by man in the laboratory. Examples of native complement proteins include C1q, C1r, C1s, C2, C3, C4, Factor B, Factor D, properdin, C5, C6, C7, C6, and C9.

Generally, native complement proteins are inactive and acquire activity upon activation. Activation can require activation cleavage, maturation cleavage and/or complex formation with other proteins. An exception to this is Factor I and Factor D which have enzymatic activity in their native form. In some examples, activation of a native complement protein occurs following cleavage of the protein. For example, complement zymogens such as C2 and Factor B are proteases which are themselves activated by protease cleavage such that cleavage of C2 by the protease C1s generates

C2b which associates with C4b to form the proteolytically active C4b2b (C3 convertase) and cleavage of Factor B by the protease Factor D generates Bb which associates with C3b to form the proteolytically active alternative C3 convertase, C3bBb. In another example, cleavage of an inactive native complement protein results in changes in the structural stability of a protein resulting in activation of the protein. For example, C3 and C4 contain an internal thioester bond which in the native protein is stable, but can become highly reactive and activated following conformational changes that result from cleavage of the protein. Thus, the cleavage products of C3 and C4 are biologically active. Activation of C3 and C4 also can occur spontaneously in the absence of cleavage. It is the spontaneous conversion of the thioester bond in native C3 that is an initiating event of the alternative pathway of complement. In other example, activation of a native complement protein occurs following the release of a complexed regulatory molecule that inhibits the activity of an otherwise active native complement protein. For example, C1inh binds to and inactivates C1s and C1r, unless they are in complex with C1q.

As used herein, maturation cleavage is a general term that refers to any cleavage required for activation of a zymogen. This includes cleavage that leads to a conformational change resulting in activity (*i.e.* activation cleavage). It also includes cleavage in which a critical binding site is exposed or a steric hindrance is exposed or an inhibitory segment is removed or moved.

As used herein, altered form of a complement protein refers to a complement protein that is present in a non-native form resulting from modifications in its molecular structure. For example, C3 reaction of the thioester with water can occur in the absence of convertase cleavage, giving a hydrolyzed inactive form of C3 and C4 termed iC3 and iC4. In another example, anaphylatoxins including C3a, C5a, and C4a can be desarginated by carboxypeptidase N into more stable, less active forms.

As used herein, a "fragment" or "cleavage product" of a complement protein is a subset of a complement protein that contains a portion of the polypeptide sequence of a native complement protein. A fragment of a complement protein usually results following the activation of any one or more, such 1, 2 or 3, of the complement cascades. Generally, a fragment results from the proteolytic cleavage of a native

complement protein. For example, Factor B is enzymatically cleaved by Factor D, resulting in two fragments: Ba which constitutes the N-terminal portion of B; and Bb which constitutes the C-terminal portion and contains the serine protease site. A fragment of a complement protein also results from the proteolytic cleavage of another fragment of a complement protein. For example, C3b, a fragment generated from the cleavage of C3, is cleaved by Factor I to generate the fragments iC3b and C3f. Generally cleavage products of complement proteins are biologically active products and function as cleavage effector molecules of the complement system. Hence a fragment or portion of complement protein includes cleavage products of complement proteins and also portions of the proteins that retain or exhibit at least one activity.

As used herein, "cleavage effector molecules" or "cleavage effector proteins" refers to the active cleavage products generated as a result of the triggered-enzyme cascade of the complement system. A cleavage effector molecule, a fragment or cleavage product resulting from complement activation can contribute to any of one or more of the complement-mediated functions or activities, which include opsonization, anaphylaxis, cell lysis and inflammation. Examples of cleavage or effector molecules include, but are not limited to, C3a, C3b, C4a, C4b, C5a, C5b-9, and Bb. Cleavage effector molecules of the complement system, by virtue of participation in the cascade, exhibit activities that include stimulating inflammation, facilitating antigen phagocytosis, and lysing some cells directly. Complement cleavage products promote or participate in the activation of the complement pathways.

As used herein, anaphylatoxins (such as, for example, C3a, C4a or C5a) are cleavage effector proteins that trigger degranulation of (release of substances from) mast cells or basophils, which participate in the inflammatory response, particularly as part of defense against parasites. If the degranulation is too strong, it can cause allergic reactions. Anaphylatoxins also indirectly mediate spasms of smooth muscle cells (such as bronchospasms), an increase in permeability of blood capillaries, and chemotaxis.

As used herein, chemotaxis refers to receptor-mediated movement of leukocytes towards a chemoattractant typically in the direction of the increasing concentration thereof, such as in the direction of increasing concentration of an anaphylatoxin.

As used herein, opsonization refers to the alteration of the surface of a pathogen or other particle so that it can be ingested by phagocytes. A protein that binds or alters the surface of a pathogen is termed an opsonin. Antibody and complement proteins opsonize extracellular bacteria for uptake and destruction by phagocytes such as neutrophils and macrophages.

As used herein, cell lysis refers to the breaking open of a cell by the destruction of its wall or membrane. Hemolysis of red blood cells is a measure of cell lysis.

As used herein, "proteases," "proteinases" and "peptidases" are interchangeably used to refer to enzymes that catalyze the hydrolysis of covalent peptidic bonds. These designations include zymogen forms and activated single-, two- and multiple-chain forms thereof. For clarity, reference to proteases refer to all forms. Proteases include, for example, serine proteases, cysteine proteases, aspartic proteases, threonine and metallo-proteases depending on the catalytic activity of their active site and mechanism of cleaving peptide bonds of a target substrate.

As used herein, a zymogen refers to a protease that is activated by proteolytic cleavage, including maturation cleavage, such as activation cleavage, and/or complex formation with other protein(s) and/or cofactor(s). A zymogen is an inactive precursor of a proteolytic enzyme. Such precursors are generally larger, although not necessarily larger, than the active form. With reference to serine proteases, zymogens are converted to active enzymes by specific cleavage, including catalytic and autocatalytic cleavage, or by binding of an activating co-factor, which generates an active enzyme. A zymogen, thus, is an enzymatically inactive protein that is converted to a proteolytic enzyme by the action of an activator. Cleavage can be effected autocatalytically. A number of complement proteins are zymogens; they are inactive, but become cleaved and activated upon the initiation of the complement system following infection. Zymogens, generally, are inactive and can be converted

to mature active polypeptides by catalytic or autocatalytic cleavage of the proregion from the zymogen.

As used herein, a "proregion," "propeptide," or "pro sequence," refers to a region or a segment that is cleaved to produce a mature protein. This can include segments that function to suppress enzymatic activity by masking the catalytic machinery and thus preventing formation of the catalytic intermediate (*i.e.*, by sterically occluding the substrate binding site). A proregion is a sequence of amino acids positioned at the amino terminus of a mature biologically active polypeptide and can be as little as a few amino acids or can be a multidomain structure.

As used herein, an activation sequence refers to a sequence of amino acids in a zymogen that is the site required for activation cleavage or maturation cleavage to form an active protease. Cleavage of an activation sequence can be catalyzed autocatalytically or by activating partners.

Activation cleavage is a type of maturation cleavage in which a conformational change required for activity occurs. This is a classical activation pathway, for example, for serine proteases in which a cleavage generates a new N-terminus which interacts with the conserved regions of catalytic machinery, such as catalytic residues, to induce conformational changes required for activity. Activation can result in production of multi-chain forms of the proteases. In some instances, single chain forms of the protease can exhibit proteolytic activity as a single chain.

As used herein, domain refers to a portion of a molecule, such as proteins or the encoding nucleic acids, that is structurally and/or functionally distinct from other portions of the molecule and is identifiable.

As used herein, a protease domain is the catalytically active portion of a protease. Reference to a protease domain of a protease includes the single, two- and multi-chain forms of any of these proteins. A protease domain of a protein contains all of the requisite properties of that protein required for its proteolytic activity, such as for example, its catalytic center.

As used herein, a catalytically active portion of a protease refers to the protease domain, or any fragment or portion thereof that retains protease activity. Significantly, at least *in vitro*, the single chain forms of the proteases and catalytic

domains or proteolytically active portions thereof (typically C-terminal truncations) exhibit protease activity.

As used herein, a "nucleic acid encoding a protease domain or catalytically active portion of a protease" refers to a nucleic acid encoding only the recited single chain protease domain or active portion thereof, and not the other contiguous portions of the protease as a continuous sequence.

As used herein, recitation that a polypeptide consists essentially of the protease domain means that the only portion of the polypeptide is a protease domain or a catalytically active portion thereof. The polypeptide can optionally, and generally will, include additional non-protease-derived sequences of amino acids.

As used herein, "S1-S4" refers to amino acid residues that form the binding sites for P1-P4 residues of a substrate (see, *e.g.*, Schecter and Berger (1967) *Biochem Biophys Res Commun* 27:157-162). Each of S1-S4 contains one, two or more residues, which can be non-contiguous. These sites are numbered sequentially from the recognition site N-terminal to the site of proteolysis, referred to as the scissile bond.

As used herein, the terms "P1-P4" and "P1'-P4'" refer to the residues in a substrate peptide that specifically interact with the S1-S4 residues and S1'-S4' residues, respectively, and are cleaved by the protease. P1-P4 refer to the residue positions on the N-terminal side of the cleavage site; P1'-P4' refer to the residue positions to the C-terminal side of the cleavage site. Amino acid residues are labeled from N to C termini of a polypeptide substrate (Pi, ..., P3, P2, P1, P1', P2', P3', ..., Pj). The respective binding subsites are labeled (Si,..., S3, S2, S1, S1', S2', S3',..., Sj). The cleavage is catalyzed between P1 and P1.'

As used herein, a "binding pocket" refers to the residue or residues that interact with a specific amino acid or amino acids on a substrate. A "specificity pocket" is a binding pocket that contributes more energy than the others (the most important or dominant binding pocket). Typically, the binding step precedes the formation of the transition state that is necessary for the catalytic process to occur. S1-S4 and S1'- S4' amino acids make up the substrate sequence binding pocket and facilitate substrate recognition by interaction with P1-P4 and P1'-P4'amino acids of a

peptide, polypeptide or protein substrate, respectively. Whether a protease interacts with a substrate is a function of the amino acids in the S1-S4 and S1'-S4' positions. If the amino acids in any one or more of the S1, S2, S3, S4, S1', S2', S3' and S4' subsites interact with or recognize any one or more of the amino acids in the P1, P2, P3, P4, P1', P2', P3' and P4' sites in a substrate, then the protease can cleave the substrate. A binding pocket positions a target amino acid with a protease so that catalysis of a peptide bond and cleavage of a substrate is achieved. For example, serine proteases typically recognize P4-P2' sites in a substrate; others proteases can have extended recognition beyond P4-P2'.

As used herein, amino acids that "contribute to extended substrate specificity" refers to those residues in the active site cleft in addition to the specificity pocket. These amino acids include the S1-S4, S1'-S4' residues in a protease.

As used herein, secondary sites of interaction are outside the active site cleft. These can contribute to substrate recognition and catalysis. These amino acids include amino acids that can contribute second and third shell interactions with a substrate. For example, loops in the structure of a protease surrounding the S1-S4. S1'-S4' amino acids play a role in positioning P1-P4, P1'-P4' amino acids in the substrate thereby registering the scissile bond in the active site of a protease.

As used herein, active site of a protease refers to the substrate binding site where catalysis of the substrate occurs. The structure and chemical properties of the active site allow the recognition and binding of the substrate and subsequent hydrolysis and cleavage of the scissile bond in the substrate. The active site of a protease contains amino acids that contribute to the catalytic mechanism of peptide cleavage as well as amino acids that contribute to substrate sequence recognition, such as amino acids that contribute to extended substrate binding specificity.

As used herein, a catalytic triad of a serine or cysteine protease refers to a combination of three amino acids that are in the active site of a serine or cysteine protease and contribute to the catalytic mechanism of peptide cleavage. Generally, a catalytic triad is found in serine proteases and provides an active nucleophile and acid/base catalysis. The catalytic triad of serine proteases contains three amino acids,

which in chymotrypsin are Asp^{102}, His^{57}, and Ser^{195}. These residues are critical for the catalytic efficiency of a serine protease.

As used herein, the "substrate recognition site" or "cleavage sequence" refers to the sequence recognized by the active site of a protease that is cleaved by a protease. Typically, for example, for a serine protease, a cleavage sequence is made up of the P1-P4 and P1'-P4' amino acids in a substrate, where cleavage occurs after the P1 position. Typically, a cleavage sequence for a serine protease is six residues in length to match the extended substrate specificity of many proteases, but can be longer or shorter depending upon the protease. For example, the substrate recognition site or cleavage sequence of MT-SP1 required for autocatalysis is RQARVV, where R is at the P4 position, Q is at the P3 position, A is at the P2 position and R is at the P1 position. Cleavage in MT-SP1 occurs after position R followed by the sequence VVGG.

As used herein, target substrate refers to a substrate that is cleaved by a protease. Typically, the target substrate is specifically cleaved at its substrate recognition site by a protease. Minimally, a target substrate includes the amino acids that make up the cleavage sequence. Optionally, a target substrate includes a peptide containing the cleavage sequence and any other amino acids. A full-length protein, allelic variant, isoform, or any portion thereof, containing a cleavage sequence recognized by a protease, is a target substrate for that protease. For example, for purposes herein in which complement inactivation is intended, a target substrate is any one or more, such as for example, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40 or more, complement proteins, or any portion or fragment thereof of a complement protein containing a cleavage sequence recognized by a protease. Such target substrates can be purified proteins, or can be present in a mixture, such as a mixture *in vitro* or a mixture *in vivo*. Mixtures can include, for example, blood or serum, or other tissue fluids. Additionally, a target substrate includes a peptide or protein containing an additional moiety that does not affect cleavage of the substrate by a protease. For example, a target substrate can include a four amino acid peptide or a full-length protein chemically linked to a fluorogenic moiety. The proteases can be modified to exhibit greater substrate specificity for a target substrate.

As used herein, cleavage refers to the breaking of peptide bonds by a protease. The cleavage site motif for a protease involves residues N- and C-terminal to the scissile bond (the unprimed and primed sides, respectively, with the cleavage site for a protease defined as ... P3-P2-P1-P1'-P2'-P3' ..., and cleavage occurs between the P1 and P1' residues). Typically, cleavage of a substrate is an activating cleavage or an inhibitory cleavage. An activating cleavage refers to cleavage of a polypeptide from an inactive form to an active form. This includes, for example, cleavage of a zymogen to an active enzyme, and/or cleavage of a progrowth factor into an active growth factor. For example, MT-SP1 can auto-activate by cleaving a target substrate at the P1-P4 sequence of RQAR. An activating cleavage also is cleavage whereby a protein is cleaved into one or more proteins that themselves have activity. For example, the complement system is an irreversible cascade of proteolytic cleavage events whose termination results in the formation of multiple effector molecules that stimulate inflammation, facilitate antigen phagocytosis, and lyse some cells directly. Thus, cleavage of C3 by convertase into C3a and C3b is an activation cleavage.

As used herein, an inhibitory cleavage is cleavage of a protein into one or more degradation products that are not functional. Inhibitory cleavage results in the diminishment or reduction of an activity of a protein. Typically, a reduction of an activity of a protein reduces the pathway or process for which the protein is involved. In one example, the cleavage of any one or more complement proteins that is an inhibitory cleavage results in the concomitant reduction or inhibition of any one or more of the classical, lectin, or alternative functional pathways of complement. To be inhibitory, the cleavage reduces activity by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99.9% or more compared to a native form of the protein. The percent cleavage of a protein that is required for the cleavage to be inhibitory varies among proteins but can be determined by assaying for an activity of the protein.

As used herein, reference to a protease that cleaves VEGF or a VEGFR refers to a protease that is modified to cleave VEGF or a VEGFR or that in its native form cleaves VEGF or a VEGFR to thereby reduce or inactivate signaling of the VEGF or VEGFR complex, particularly cell proliferation signaling that can be manifested as a

biological effect such as angiogenesis, particular undesired angiogenesis. Cleavage of VEGF or VEGFR by a protease can be determined by assaying for the activity of a VEGF or VEGFR using any method or assay known to one of skill in the art to assess VEGF or VEGFR function.

As used herein, reference to a protease (modified or unmodified) that does not cleave VEGF or a VEGFR refers to a protease that does not reduce or inactivate signaling of the VEGF or a VEGFR complex. In particular, for purposes herein, the protease has greater substrate specificity or activity to a target substrate (*i.e.* a complement protein), such as or about 1-fold, 1.5-fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, 200-fold, 300-fold, 400-fold or more, than for a VEGF or a VEGFR protein or a peptide substrate that contains the corresponding cleavage sequence (*i.e.* RRVR). For purposes herein, comparison of cleavage of a complement protein with a VEGF or VEGFR protein or peptide substrate is under the same reaction conditions as a protease cleaves a complement protein.

As used herein, the "scaffold" or "protease scaffold" refers to a prototype protease that can be modified to alter its target specificity. Scaffolds include wildtype proteases, allelic variants and isoforms. They can serve as the starting material for modification to produce a protease that has a targeted specificity.

As used herein, a "modified protease," or "mutein protease" refers to a protease polypeptide (protein) that has one or more modifications in primary sequence compared to a scaffold protease. The one or more mutations can be one or more amino acid replacements (substitutions), insertions, deletions and any combination thereof. A modified protease polypeptide includes those with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more modified positions. A modified protease can be a full-length scaffold protease, or can be a catalytically active portion thereof of a modified full length scaffold protease as long as the modified protease contains modifications in regions that alter the activity or substrate specificity of the protease and the protease is proteolytically active. Generally, these mutations change the specificity and activity of the scaffold proteases for cleavage of any one or more of the complement proteins. In addition to containing modifications in regions that alter the substrate specificity of a protease, a modified protease also can tolerate other

modifications in regions that are non-essential to the substrate specificity of a protease. Hence, a modified protease typically has 60%, 70%, 80 %, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to a corresponding sequence of amino acids of a wildtype or scaffold protease. A modified full-length protease or a catalytically active portion thereof of a modified protease can include proteases that are fusion proteins as long as the fusion itself does not alter substrate specificity of a protease.

As used herein, chymotrypsin numbering refers to the amino acid numbering of a mature chymotrypsin polypeptide of SEQ ID NO:8. Alignment of a protease domain of another protease, such as for example the protease domain of MT-SP1, can be made with chymotrypsin. In such an instance, the amino acids of MT-SP1 that correspond to amino acids of chymotrypsin are given the numbering of the chymotrypsin amino acids. Corresponding positions can be determined by such alignment by one of skill in the art using manual alignments or by using the numerous alignment programs available (for example, BLASTP). Corresponding positions also can be based on structural alignments, for example by using computer simulated alignments of protein structure. Recitation that amino acids of a polypeptide correspond to amino acids in a disclosed sequence refers to amino acids identified upon alignment of the polypeptide with the disclosed sequence to maximize identity or homology (where conserved amino acids are aligned) using a standard alignment algorithm, such as the GAP algorithm. For example, upon alignment of the serine protease domain of MT-SP1 (SEQ ID NO:10) with mature chymotrypsin, V at position 1 in MT-SP1 is given the chymotrypsin numbering of V16. Subsequent amino acids are numbered accordingly. In one example, an F at amino acid position 708 of full-length MT-SP1 (SEQ ID NO:2) or at position 94 of the protease domain of MT-SP1 (SEQ ID NO:10), corresponds to F99 based on chymotrypsin numbering. Where a residue exists in a protease, but is not present in chymotrypsin, the amino acid residue is given a letter notation. For example, residues in chymotrypsin that are part of a loop with amino acid 60 based on chymotrypsin numbering, but are inserted in the MT-SP1 sequence compared to chymotrypsin, are referred to for example as Asp60b or Arg60c.

As used herein, "inhibiting complement activation" or "complement inactivation" refers to the reduction or decrease of a complement-mediated function or activity of any one or more of the complement pathways by a protease or in the activity of any of the proteins in a pathway. A function or activity of complement can occur *in vitro* or *in vivo*. Exemplary functions of complement that can be assayed and that are described herein include hemolytic assays, and assays to measure any one or more of the complement effector molecules such as by SDS PAGE followed by Western Blot or Coomassie Brilliant Blue staining or by ELISA. A protease can inhibit complement activation by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more. In other embodiments, complement activation is inhibited by a protease by 40%, 50%, 60%, 70%, 80%, 85%, 90%, 95% or 99.9% compared to the activity of complement in the absence of a protease.

As used herein, specificity for a target substrate refers to a preference for cleavage of a target substrate by a protease compared to a another substrate, referred to as a non-target substrate. Specificity is reflected in the specificity constant (k_{cat}/K_m), which is a measure of the affinity of a protease for its substrate and the efficiency of the enzyme.

As used herein, a specificity constant for cleavage is (k_{cat}/K_m), wherein K_m is the Michaelis-Menton constant ([S] at one half V_{max}) and k_{cat} is the $V_{max}/[E_T]$, where E_T is the final enzyme concentration. The parameters k_{cat}, K_m and k_{cat}/K_m can be calculated by graphing the inverse of the substrate concentration versus the inverse of the velocity of substrate cleavage, and fitting to the Lineweaver-Burk equation ($1/velocity=(K_m/V_{max})(1/[S]) + 1/V_{max}$; where $V_{max}=[E_T]k_{cat}$). Any method to determine the rate of increase of cleavage over time in the presence of various concentrations of substrate can be used to calculate the specificity constant. For example, a substrate is linked to a fluorogenic moiety, which is released upon cleavage by a protease. By determining the rate of cleavage at different enzyme concentrations, k_{cat} can be determined for a particular protease. The specificity constant can be used to determine the site specific preferences of an amino acid in any one or more of the S1-S4 pockets of a protease for a concomitant P1-P4 amino acid in a substrate using standard methods in the art, such as a positional scanning

combinatorial library (PS-SCL). Additionally, the specificity constant also can be used to determine the preference of a protease for one target substrate over another substrate.

As used herein, substrate specificity refers to the preference of a protease for one target substrate over another. Substrate specificity can be measured as a ration of specificity constants.

As used herein, a substrate specificity ratio is the ratio of specificity constants and can be used to compare specificities of two or more proteases or a protease for two more substrates. For example, substrate specificity of a protease for competing substrates or of competing proteases for a substrate can be compared by comparing k_{cat}/K_m. For example, a protease that has a specificity constant of 2×10^6 $M^{-1}sec^{-1}$ for a target substrate and 2×10^4 $M^{-1}sec^{-1}$ for a non-target substrate is more specific for the target substrate. Using the specificity constants from above, the protease has a substrate specificity ratio of 100 for the target protease.

As used herein, preference or substrate specificity for a target substrate can be expressed as a substrate specificity ratio. The particular value of the ratio that reflects a preference is a function of the substrates and proteases at issue. A substrate specificity ratio that is greater than 1 signifies a preference for a target substrate and a substrate specificity less than 1 signifies a preference for a non-target substrate. Generally, a ratio of at least or about 1 reflects a sufficient difference for a protease to be considered a candidate therapeutic.

As used herein, altered specificity refers to a change in substrate specificity of a modified protease compared to a starting scaffold protease. Generally, the change in specificity is a reflection of the change in preference of a modified protease for a target substrate compared to a wildtype substrate of the scaffold protease (herein referred to as a non-target substrate). Typically, modified proteases provided herein exhibit increased substrate specificity for any one or more of the complement proteins compared to the substrate specificity of a scaffold protease. For example, a modified protease that has a substrate specificity ratio of 100 for a target substrate versus a non-target substrate exhibits a 10-fold increased specificity compared to a scaffold protease with a substrate specificity ratio of 10. In another example, a modified

protease that has a substrate specificity ratio of 1 compared to a ratio of 0.1, exhibits a 10-fold increase in substrate specificity. To exhibit increased specificity compared to a scaffold protease, a modified protease has a 1.5-fold, 2-fold, 5-fold, 10-fold, 50-fold, 100-fold, 200-fold, 300-fold, 400-fold, 500-fold or more greater substrate specificity for any one of more of the complement proteins.

As used herein, "selectivity" can be used interchangeably with specificity when referring to the ability of a protease to choose and cleave one target substrate from among a mixture of competing substrates. Increased selectivity of a protease for a target substrate compared to any other one or more target substrates can be determined, for example, by comparing the specificity constants of cleavage of the target substrates by a protease. For example, if a protease has a specificity constant of cleavage of 2×10^6 $M^{-1}sec^{-1}$ for a target substrate and 2×10^4 $M^{-1}sec^{-1}$ for any other one of more substrates, the protease is more selective for the former target substrate.

As used herein, activity refers to a functional activity or activities of a polypeptide or portion thereof associated with a full-length (complete) protein. Functional activities include, but are not limited to, biological activity, catalytic or enzymatic activity, antigenicity (ability to bind to or compete with a polypeptide for binding to an anti-polypeptide antibody), immunogenicity, ability to form multimers, and the ability to specifically bind to a receptor or ligand for the polypeptide.

As used herein, a functional activity with reference to a complement protein refers to a complement-mediated function including, but not limited to, anaphylaxis, opsonization, chemotaxis, or cell lysis. Nonlimiting assays for testing activities of complement include hemolysis of red blood cells, and detection of complement effector molecules such as by ELISA or SDS-PAGE.

As used herein, catalytic activity or cleavage activity refers to the activity of a protease as assessed in *in vitro* proteolytic assays that detect proteolysis of a selected substrate. Cleavage activity can be measured by assessing catalytic efficiency of a protease.

As used herein, activity towards a target substrate refers to cleavage activity and/or functional activity, or other measurement that reflects the activity of a protease on or towards a target substrate. A functional activity of a complement protein target

substrate by a protease can be measured by assessing an IC50 in a complement assay such as red blood cell lysis, or other such assays known by one of skill in the art or provided herein to assess complement activity. Cleavage activity can be measured by assessing catalytic efficiency of a protease. For purposes herein, an activity is increased if a protease exhibits greater proteolysis or cleavage of a target substrate and/or modulates (*i.e.* activates or inhibits) a functional activity of a complement protein as compared to in the absence of the protease.

As used herein, serine proteases or serine endopeptidases refers to a class of peptidases, which are characterized by the presence of a serine residue in the active center of the enzyme. Serine proteases participate in a wide range of functions in the body, including blood clotting and inflammation, as well as functioning as digestive enzymes in prokaryotes and eukaryotes. The mechanism of cleavage by serine proteases is based on nucleophilic attack of a targeted peptidic bond by a serine. Cysteine, threonine or water molecules associated with aspartate or metals also can play this role. Aligned side chains of serine, histidine and aspartate form a catalytic triad common to most serine proteases. The active site of serine proteases is shaped as a cleft where the polypeptide substrate binds.

As used herein, a complement protease refers to a protease that is involved in the generation and amplification of complement cascade reactions in any of the complement pathways. These proteases include the serine protease factor I, factor D, MBL-associated serine protease (MASP)-2, MASP-1, C1s, C1r, factor B, C2, and the convertases and any other protease that occurs in a complement pathway whereby complement activation is effected. In particular, complement proteases are any unmodified complement proteases, including factor I, factor D, MASP-2, MASP-1, C1s, C1r, factor B and C2.

As used herein, a non-complement protease is any protease that is not normally part of any one or more of the complement pathways.

As used herein, MT-SP1 refers to a serine protease that is part of the S1 peptidase family of serine proteases (also containing trypsin and chymotrypsin) based on the location of the Ser, His, and Lys active site residues. MT-SP1 is characterized by a transmembrane domain, two CUB domains, four LDLR repeats, and a serine

protease domain (or peptidase S1 domain) that is highly conserved among all members of the peptidase S1 family of serine proteases, such as for example with chymotrypsin. The sequence of an exemplary MT-SP1 is set forth in SEQ ID NO: 2. The protease domain occurs between and includes amino acids 615-854.

Reference to an MT-SP1 protease includes a full-length MT-SP1 or any catalytically active portion thereof and includes allelic variants and species variants and variants encoded by splice variants. An MT-SP1 protease occurs as a single chain zymogen, and as an activated two-chain polypeptide. Reference to MT-SP1 includes active single-chain and two-chain forms thereof. Of particular interest are MT-SP1 proteases of mammalian, including human, origin. An MT-SP1 protease also can include those of rat or mouse origin. Those of skill in this art recognize that, in general, single amino acid substitutions in non-essential regions of a polypeptide do not substantially alter biological activity (see, e.g., Watson et al. Molecular Biology of the Gene, 4th Edition, 1987, The Benjamin/Cummings Pub. co., p.224). Sequences of encoding nucleic molecules and the encoded amino acid sequences of exemplary MT-SP1 proteases of human origin and/or catalytically active domains thereof are set forth in SEQ ID NOS: 1, 2, 9 and 10. Exemplary MT-SP1 polypeptides of non-human origin are those having amino acid sequences such as in mice (*Mus musculus,* SEQ ID NO: 449) and rats (*Rattus norvegicus*, SEQ ID NO: 450). Herein, an MT-SP1 protease can be a scaffold MT-SP1.

As used herein, reference to a "catalytically active portion thereof" of an MT-SP1 protease refers to the protease domain, or any fragment or portion thereof that retains protease activity. For example, a catalytically active portion of an MT-SP1 can be an MT-SP1 protease domain including an isolated single chain form of the protease domain or an activated two-chain form.

As used herein, a modified MT-SP1 protease refers to a protease that exhibits altered activity, such as altered substrate specificity, compared to the scaffold or unmodified form. Such proteases include 1, 2, 3, 4, 5, 6, 7, 8, 9 , 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more modifications (*i.e.* changes in amino acids) compared to a scaffold MT-SP1 such that an activity, such as substrate specificity or selectivity, of the MT-SP1 protease for cleaving a complement protein is altered. A modified

MT-SP1 can be a full-length scaffold MT-SP1, or can be a portion thereof of a full length scaffold protease, as long as the modified protease contains modifications in regions that alter the activity or substrate specificity of the protease and the protease is proteolytically active. A modified MT-SP1 protease also can include other modifications in regions that do not impact on substrate specificity of the protease. Hence, a modified MT-SP1 protease typically has 60%, 70%, 80 %, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to a corresponding sequence of amino acids of a wildtype or scaffold MT-SP1. A modified full-length MT-SP1 protease or a catalytically active portion thereof of a modified MT-SP1 can include proteases that are fusion proteins as long as the fusion protein possesses the target specificity.

As used herein, a human protein is one encoded by a nucleic acid molecule, such as DNA, present in the genome of a human, including all allelic variants and conservative variations thereof. A variant or modification of a protein is a human protein if the modification is based on the wildtype or prominent sequence of a human protein.

As used herein, the residues of naturally occurring α-amino acids are the residues of those 20 α-amino acids found in nature which are incorporated into protein by the specific recognition of the charged tRNA molecule with its cognate mRNA codon in humans.

As used herein, non-naturally occurring amino acids refer to amino acids that are not genetically encoded.

As used herein, nucleic acids include DNA, RNA and analogs thereof, including peptide nucleic acids (PNA) and mixtures thereof. Nucleic acids can be single or double-stranded. When referring to probes or primers, which are optionally labeled, such as with a detectable label, such as a fluorescent or radiolabel, single-stranded molecules are contemplated. Such molecules are typically of a length such that their target is statistically unique or of low copy number (typically less than 5, generally less than 3) for probing or priming a library. Generally a probe or primer contains at least 14, 16 or 30 contiguous nucleotides of sequence complementary to or

identical to a gene of interest. Probes and primers can be 10, 20, 30, 50, 100 or more nucleic acids long.

As used herein, a peptide refers to a polypeptide that is from 2 to 40 amino acids in length.

As used herein, the amino acids which occur in the various sequences of amino acids provided herein are identified according to their known, three-letter or one-letter abbreviations (Table 1). The nucleotides which occur in the various nucleic acid fragments are designated with the standard single-letter designations used routinely in the art.

As used herein, an "amino acid" is an organic compound containing an amino group and a carboxylic acid group. A polypeptide contains two or more amino acids. For purposes herein, amino acids include the twenty naturally-occurring amino acids, non-natural amino acids and amino acid analogs (i.e., amino acids wherein the α-carbon has a side chain).

As used herein, the "amino acids," which occur in the various amino acid sequences appearing herein, are identified according to their well-known, three-letter or one-letter abbreviations (see Table 1). The nucleotides, which occur in the various DNA fragments, are designated with the standard single-letter designations used routinely in the art.

As used herein, "amino acid residue" refers to an amino acid formed upon chemical digestion (hydrolysis) of a polypeptide at its peptide linkages. The amino acid residues described herein are presumed to be in the "L" isomeric form. Residues in the "D" isomeric form, which are so designated, can be substituted for any L-amino acid residue as long as the desired functional property is retained by the polypeptide. NH_2 refers to the free amino group present at the amino terminus of a polypeptide. COOH refers to the free carboxy group present at the carboxyl terminus of a polypeptide. In keeping with standard polypeptide nomenclature described in *J. Biol. Chem.*, 243: 3552-3559 (1969), and adopted 37 C.F.R. §§ 1.821-1.822, abbreviations for amino acid residues are shown in Table 1:

Table 1 – Table of Correspondence

SYMBOL	

1-Letter	3-Letter	AMINO ACID
Y	Tyr	Tyrosine
G	Gly	Glycine
F	Phe	Phenylalanine
M	Met	Methionine
A	Ala	Alanine
S	Ser	Serine
I	Ile	Isoleucine
L	Leu	Leucine
T	Thr	Threonine
V	Val	Valine
P	Pro	proline
K	Lys	Lysine
H	His	Histidine
Q	Gln	Glutamine
E	Glu	glutamic acid
Z	Glx	Glu and/or Gln
W	Trp	Tryptophan
R	Arg	Arginine
D	Asp	aspartic acid
N	Asn	asparagines
B	Asx	Asn and/or Asp
C	Cys	Cysteine
X	Xaa	Unknown or other

It should be noted that all amino acid residue sequences represented herein by formulae have a left to right orientation in the conventional direction of amino-terminus to carboxyl-terminus. In addition, the phrase "amino acid residue" is broadly defined to include the amino acids listed in the Table of Correspondence (Table 1) and modified and unusual amino acids, such as those referred to in 37 C.F.R. §§ 1.821-1.822, and incorporated herein by reference. Furthermore, it should be noted that a dash at the beginning or end of an amino acid residue sequence indicates a peptide bond to a further sequence of one or more amino acid residues, to an amino-terminal group such as NH_2 or to a carboxyl-terminal group such as COOH.

As used herein, "naturally occurring amino acids" refer to the 20 L-amino acids that occur in polypeptides.

As used herein, "non-natural amino acid" refers to an organic compound that has a structure similar to a natural amino acid but has been modified structurally to mimic the structure and reactivity of a natural amino acid. Non-naturally occurring amino acids thus include, for example, amino acids or analogs of amino acids other

than the 20 naturally-occurring amino acids and include, but are not limited to, the D-isostereomers of amino acids. Exemplary non-natural amino acids are described herein and are known to those of skill in the art.

As used herein, an isokinetic mixture is one in which the molar ratios of amino acids has been adjusted based on their reported reaction rates (see, *e.g.*, Ostresh et al., (1994) Biopolymers 34:1681).

As used herein, a DNA construct is a single or double stranded, linear or circular DNA molecule that contains segments of DNA combined and juxtaposed in a manner not found in nature. DNA constructs exist as a result of human manipulation, and include clones and other copies of manipulated molecules.

As used herein, a DNA segment is a portion of a larger DNA molecule having specified attributes. For example, a DNA segment encoding a specified polypeptide is a portion of a longer DNA molecule, such as a plasmid or plasmid fragment, which, when read from the 5' to 3' direction , encodes the sequence of amino acids of the specified polypeptide.

As used herein, the term ortholog means a polypeptide or protein obtained from one species that is the functional counterpart of a polypeptide or protein from a different species. Sequence differences among orthologs are the result of speciation.

As used herein, the term polynucleotide means a single- or double-stranded polymer of deoxyribonucleotides or ribonucleotide bases read from the 5' to the 3' end. Polynucleotides include RNA and DNA, and can be isolated from natural sources, synthesized *in vitro*, or prepared from a combination of natural and synthetic molecules. The length of a polynucleotide molecule is given herein in terms of nucleotides (abbreviated "nt") or base pairs (abbreviated "bp"). The term nucleotides is used for single- and double-stranded molecules where the context permits. When the term is applied to double-stranded molecules it is used to denote overall length and will be understood to be equivalent to the term base pairs. It will be recognized by those skilled in the art that the two strands of a double-stranded polynucleotide can differ slightly in length and that the ends thereof can be staggered; thus all nucleotides within a double-stranded polynucleotide molecule can not be paired. Such unpaired ends will, in general, not exceed 20 nucleotides in length.

As used herein, a protease polypeptide is a polypeptide having an amino acid sequence corresponding to any one of the scaffold or modified proteases described herein.

As used herein, "similarity" between two proteins or nucleic acids refers to the relatedness between the sequence of amino acids of the proteins or the nucleotide sequences of the nucleic acids. Similarity can be based on the degree of identity and/or homology of sequences of residues and the residues contained therein. Methods for assessing the degree of similarity between proteins or nucleic acids are known to those of skill in the art. For example, in one method of assessing sequence similarity, two amino acid or nucleotide sequences are aligned in a manner that yields a maximal level of identity between the sequences. "Identity" refers to the extent to which the amino acid or nucleotide sequences are invariant. Alignment of amino acid sequences, and to some extent nucleotide sequences, also can take into account conservative differences and/or frequent substitutions in amino acids (or nucleotides). Conservative differences are those that preserve the physico-chemical properties of the residues involved. Alignments can be global (alignment of the compared sequences over the entire length of the sequences and including all residues) or local (the alignment of a portion of the sequences that includes only the most similar region or regions).

"Identity" per se has an art-recognized meaning and can be calculated using published techniques. (See, *e.g.*: *Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data*, Part I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). While there exist a number of methods to measure identity between two polynucleotide or polypeptides, the term "identity" is well known to skilled artisans (Carrillo, H. & Lipman, D., *SIAM J Applied Math 48*:1073 (1988)).

As used herein, by homologous (with respect to nucleic acid and/or amino acid sequences) means about greater than or equal to 25% sequence homology, typically greater than or equal to 25%, 40%, 60%, 70%, 80%, 85%, 90% or 95% sequence homology; the precise percentage can be specified if necessary. For purposes herein the terms "homology" and "identity" are often used interchangeably, unless otherwise indicated. In general, for determination of the percentage homology or identity, sequences are aligned so that the highest order match is obtained (see, *e.g.*: *Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part I*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; Carrillo *et al.* (1988) *SIAM J Applied Math 48*:1073). By sequence homology, the number of conserved amino acids is determined by standard alignment algorithm programs, and can be used with default gap penalties established by each supplier. Substantially homologous nucleic acid molecules would hybridize typically at moderate stringency or at high stringency all along the length of the nucleic acid of interest. Also contemplated are nucleic acid molecules that contain degenerate codons in place of codons in the hybridizing nucleic acid molecule.

Whether any two molecules have nucleotide sequences or amino acid sequences that are at least 60%, 70%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% "identical" or "homologous" can be determined using known computer algorithms such as the "FASTA" program, using for example, the default parameters as in Pearson *et al.* (1988) *Proc. Natl. Acad. Sci. USA 85*:2444 (other programs include the GCG program package (Devereux, J., *et al., Nucleic Acids Research 12(I)*:387 (1984)), BLASTP, BLASTN, FASTA (Altschul, S.F., *et al., J Molec Biol 215*:403 (1990); Guide to Huge Computers, Martin J. Bishop, ed., Academic Press, San Diego, 1994, and Carrillo *et al.* (1988) *SIAM J Applied Math 48*:1073). For example, the BLAST function of the National Center for Biotechnology Information database can be used to determine identity. Other commercially or publicly available programs

include the DNAStar "MegAlign" program (Madison, WI) and the University of Wisconsin Genetics Computer Group (UWG) "Gap" program (Madison WI)). Percent homology or identity of proteins and/or nucleic acid molecules can be determined, for example, by comparing sequence information using a GAP computer program (*e.g.*, Needleman *et al.* (1970) *J. Mol. Biol.* 48:443, as revised by Smith and Waterman (1981) *Adv. Appl. Math.* 2:482). Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids), which are similar, divided by the total number of symbols in the shorter of the two sequences. Default parameters for the GAP program can include: (1) a unary comparison matrix (containing a value of 1 for identities and 0 for non-identities) and the weighted comparison matrix of Gribskov *et al.* (1986) *Nucl. Acids Res.* 14:6745, as described by Schwartz and Dayhoff, eds., *ATLAS OF PROTEIN SEQUENCE AND STRUCTURE*, National Biomedical Research Foundation, pp. 353-358 (1979); (2) a penalty of 3.0 for each gap and an additional 0.10 penalty for each symbol in each gap; and (3) no penalty for end gaps.

Therefore, as used herein, the term "identity" or "homology" represents a comparison between a test and a reference polypeptide or polynucleotide. As used herein, the term "at least 90% identical to" refers to percent identities from 90 to 99.99 relative to the reference nucleic acid or amino acid sequence of the polypeptide. Identity at a level of 90% or more is indicative of the fact that, assuming for exemplification purposes a test and reference polypeptide length of 100 amino acids are compared, no more than 10% (i.e., 10 out of 100) of the amino acids in the test polypeptide differs from that of the reference polypeptide. Similar comparisons can be made between test and reference polynucleotides. Such differences can be represented as point mutations randomly distributed over the entire length of a polypeptide or they can be clustered in one or more locations of varying length up to the maximum allowable, *e.g.* 10/100 amino acid difference (approximately 90% identity). Differences are defined as nucleic acid or amino acid substitutions, insertions or deletions. At the level of homologies or identities above about 85-90%, the result should be independent of the program and gap parameters set; such high

levels of identity can be assessed readily, often by manual alignment without relying on software.

As used herein, an aligned sequence refers to the use of homology (similarity and/or identity) to align corresponding positions in a sequence of nucleotides or amino acids. Typically, two or more sequences that are related by 50% or more identity are aligned. An aligned set of sequences refers to 2 or more sequences that are aligned at corresponding positions and can include aligning sequences derived from RNAs, such as ESTs and other cDNAs, aligned with genomic DNA sequence.

As used herein, "primer" refers to a nucleic acid molecule that can act as a point of initiation of template-directed DNA synthesis under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and a polymerization agent , such as DNA polymerase, RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. It will be appreciated that certain nucleic acid molecules can serve as a "probe" and as a "primer." A primer, however, has a 3' hydroxyl group for extension. A primer can be used in a variety of methods, including, for example, polymerase chain reaction (PCR), reverse-transcriptase (RT)-PCR, RNA PCR, LCR, multiplex PCR, panhandle PCR, capture PCR, expression PCR, 3' and 5' RACE, *in situ* PCR, ligation-mediated PCR and other amplification protocols.

As used herein, "primer pair" refers to a set of primers that includes a 5' (upstream) primer that hybridizes with the 5' end of a sequence to be amplified (e.g. by PCR) and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

As used herein, "specifically hybridizes" refers to annealing, by complementary base-pairing, of a nucleic acid molecule (e.g. an oligonucleotide) to a target nucleic acid molecule. Those of skill in the art are familiar with *in vitro* and *in vivo* parameters that affect specific hybridization, such as length and composition of the particular molecule. Parameters particularly relevant to *in vitro* hybridization further include annealing and washing temperature, buffer composition and salt concentration. Exemplary washing conditions for removing non-specifically bound nucleic acid molecules at high stringency are 0.1 x SSPE, 0.1% SDS, 65°C, and at

medium stringency are 0.2 x SSPE, 0.1% SDS, 50°C. Equivalent stringency conditions are known in the art. The skilled person can readily adjust these parameters to achieve specific hybridization of a nucleic acid molecule to a target nucleic acid molecule appropriate for a particular application.

As used herein, substantially identical to a product means sufficiently similar so that the property of interest is sufficiently unchanged so that the substantially identical product can be used in place of the product.

As used herein, it also is understood that the terms "substantially identical" or "similar" varies with the context as understood by those skilled in the relevant art.

As used herein, an allelic variant or allelic variation references any of two or more alternative forms of a gene occupying the same chromosomal locus. Allelic variation arises naturally through mutation, and can result in phenotypic polymorphism within populations. Gene mutations can be silent (no change in the encoded polypeptide) or can encode polypeptides having altered amino acid sequence. The term "allelic variant" also is used herein to denote a protein encoded by an allelic variant of a gene. Typically the reference form of the gene encodes a wildtype form and/or predominant form of a polypeptide from a population or single reference member of a species. Typically, allelic variants, which include variants between and among species, have at least 80%, 90% or greater amino acid identity with a wildtype and/or predominant form from the same species; the degree of identity depends upon the gene and whether comparison is interspecies or intraspecies. Generally, intraspecies allelic variants have at least about 80%, 85%, 90% or 95% identity or greater with a wildtype and/or predominant form, including 96%, 97%, 98%, 99% or greater identity with a wildtype and/or predominant form of a polypeptide.

As used herein, "allele," which is used interchangeably herein with ""allelic variant" refers to alternative forms of a gene or portions thereof. Alleles occupy the same locus or position on homologous chromosomes. When a subject has two identical alleles of a gene, the subject is said to be homozygous for that gene or allele. When a subject has two different alleles of a gene, the subject is said to be heterozygous for the gene. Alleles of a specific gene can differ from each other in a single nucleotide or several nucleotides, and can include substitutions, deletions and

insertions of nucleotides. An allele of a gene also can be a form of a gene containing a mutation.

As used herein, a splice variant refers to a variant produced by differential processing of a primary transcript of genomic DNA that results in more than one type of mRNA.

As used herein, modification is in reference to modification of a sequence of amino acids of a polypeptide or a sequence of nucleotides in a nucleic acid molecule and includes deletions, insertions, and replacements of amino acids and nucleotides, respectively.

For purposes herein, amino acid substitutions, deletions and/or insertions, can be made in any of the proteases and protease domains thereof provided that the resulting protein exhibits protease activity or other activity (or, if desired, such changes can be made to eliminate activity). Modifications can be made by making conservative amino acid substitutions and also non-conservative amino acid substitutions. For example, amino acid substitutions that desirably or advantageously alter properties of the proteins can be made. In one embodiment, mutations that prevent degradation of the polypeptide can be made. Many proteases cleave after basic residues, such as R and K; to eliminate such cleavage, the basic residue is replaced with a non-basic residue. Interaction of the protease with an inhibitor can be blocked while retaining catalytic activity by effecting a non-conservative change at the site of interaction of the inhibitor with the protease. Other activities also can be altered. For example, receptor binding can be altered without altering catalytic activity.

Amino acid substitutions contemplated include conservative substitutions, such as those set forth in Table 2, which do not eliminate proteolytic activity. As described herein, substitutions that alter properties of the proteins, such as removal of cleavage sites and other such sites also are contemplated; such substitutions are generally non-conservative, but can be readily effected by those of skill in the art.

Suitable conservative substitutions of amino acids are known to those of skill in this art and can be made generally without altering the biological activity, for example enzymatic activity, of the resulting molecule. Those of skill in this art

recognize that, in general, single amino acid substitutions in non-essential regions of a polypeptide do not substantially alter biological activity (see, *e.g.*, Watson *et al. Molecular Biology of the Gene*, 4th Edition, 1987, The Benjamin/Cummings Pub. co., p.224). Also included within the definition, is the catalytically active fragment of a serine protease, particularly a single chain protease portion. Conservative amino acid substitutions are made, for example, in accordance with those set forth in TABLE 2 as follows:

TABLE 2

Original residue	**Conservative substitution**
Ala (A)	Gly; Ser; Abu
Arg (R)	Lys; orn
Asn (N)	Gln; His
Cys (C)	Ser
Gln (Q)	Asn
Glu (E)	Asp
Gly (G)	Ala; Pro
His (H)	Asn; Gln
Ile (I)	Leu; Val
Leu (L)	Ile; Val
Lys (K)	Arg; Gln; Glu
Met (M)	Leu; Tyr; Ile
Ornithine	Lys; Arg
Phe (F)	Met; Leu; Tyr
Ser (S)	Thr
Thr (T)	Ser
Trp (W)	Tyr
Tyr (Y)	Trp; Phe
Val (V)	Ile; Leu; Met

Other substitutions also are permissible and can be determined empirically or in accord with known conservative substitutions.

As used herein, the term promoter means a portion of a gene containing DNA sequences that provide for the binding of RNA polymerase and initiation of transcription. Promoter sequences are commonly, but not always, found in the 5' non-coding region of genes.

As used herein, isolated or purified polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell of tissue from which the protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized.

Preparations can be determined to be substantially free if they appear free of readily detectable impurities as determined by standard methods of analysis, such as thin layer chromatography (TLC), gel electrophoresis and high performance liquid chromatography (HPLC), used by those of skill in the art to assess such purity, or sufficiently pure such that further purification would not detectably alter the physical and chemical properties, such as enzymatic and biological activities, of the substance. Methods for purification of the compounds to produce substantially chemically pure compounds are known to those of skill in the art. A substantially chemically pure compound, however, can be a mixture of stereoisomers. In such instances, further purification might increase the specific activity of the compound.

The term substantially free of cellular material includes preparations of proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the term substantially free of cellular material includes preparations of protease proteins having less that about 30% (by dry weight) of non-protease proteins (also referred to herein as a contaminating protein), generally less than about 20% of non-protease proteins or 10% of non-protease proteins or less that about 5% of non-protease proteins. When the protease protein or active portion thereof is recombinantly produced, it also is substantially free of culture medium, *i.e.*, culture medium represents less than, about, or equal to 20%, 10% or 5% of the volume of the protease protein preparation.

As used herein, the term substantially free of chemical precursors or other chemicals includes preparations of protease proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. The term includes preparations of protease proteins having less than about 30% (by dry weight), 20%, 10%, 5% or less of chemical precursors or non-protease chemicals or components.

As used herein, production by recombinant means by using recombinant DNA methods refers to the use of the well known methods of molecular biology for expressing proteins encoded by cloned DNA.

As used herein, vector (or plasmid) refers to discrete elements that are used to introduce heterologous nucleic acid into cells for either expression or replication

thereof. The vectors typically remain episomal, but can be designed to effect integration of a gene or portion thereof into a chromosome of the genome. Also contemplated are vectors that are artificial chromosomes, such as yeast artificial chromosomes and mammalian artificial chromosomes. Selection and use of such vehicles are well known to those of skill in the art.

As used herein, an expression vector includes vectors capable of expressing DNA that is operatively linked with regulatory sequences, such as promoter regions, that are capable of effecting expression of such DNA fragments. Such additional segments can include promoter and terminator sequences, and optionally can include one or more origins of replication, one or more selectable markers, an enhancer, a polyadenylation signal, and the like. Expression vectors are generally derived from plasmid or viral DNA, or can contain elements of both. Thus, an expression vector refers to a recombinant DNA or RNA construct, such as a plasmid, a phage, recombinant virus or other vector that, upon introduction into an appropriate host cell, results in expression of the cloned DNA. Appropriate expression vectors are well known to those of skill in the art and include those that are replicable in eukaryotic cells and/or prokaryotic cells and those that remain episomal or those which integrate into the host cell genome.

As used herein, vector also includes "virus vectors" or "viral vectors." Viral vectors are engineered viruses that are operatively linked to exogenous genes to transfer (as vehicles or shuttles) the exogenous genes into cells.

As used herein, an adenovirus refers to any of a group of DNA-containing viruses that cause conjunctivitis and upper respiratory tract infections in humans. As used herein, naked DNA refers to histone-free DNA that can be used for vaccines and gene therapy. Naked DNA is the genetic material that is passed from cell to cell during a gene transfer processed called transformation. In transformation, purified or naked DNA is taken up by the recipient cell which will give the recipient cell a new characteristic or phenotype.

As used herein, operably or operatively linked when referring to DNA segments means that the segments are arranged so that they function in concert for

their intended purposes, e.g., transcription initiates in the promoter and proceeds through the coding segment to the terminator.

As used herein, protein binding sequence refers to a protein or peptide sequence that is capable of specific binding to other protein or peptide sequences generally, to a set of protein or peptide sequences or to a particular protein or peptide sequence.

As used herein, epitope tag refers to a short stretch of amino acid residues corresponding to an epitope to facilitate subsequent biochemical and immunological analysis of the epitope tagged protein or peptide. Epitope tagging is achieved by adding the sequence of the epitope tag to a protein-encoding sequence in an appropriate expression vector. Epitope tagged proteins can be affinity purified using highly specific antibodies raised against the tags.

As used herein, metal binding sequence refers to a protein or peptide sequence that is capable of specific binding to metal ions generally, to a set of metal ions or to a particular metal ion.

As used herein the term assessing is intended to include quantitative and qualitative determination in the sense of obtaining an absolute value for the activity of a protease, or a domain thereof, present in the sample, and also of obtaining an index, ratio, percentage, visual or other value indicative of the level of the activity. Assessment can be direct or indirect and the chemical species actually detected need not of course be the proteolysis product itself but can for example be a derivative thereof or some further substance. For example, detection of a cleavage product of a complement protein, such as by SDS-PAGE and protein staining with Coomassie blue.

As used herein, biological activity refers to the *in vivo* activities of a compound or physiological responses that result upon *in vivo* administration of a compound, composition or other mixture. Biological activity, thus, encompasses therapeutic effects and pharmaceutical activity of such compounds, compositions and mixtures. Biological activities can be observed in *in vitro* systems designed to test or use such activities. Thus, for purposes herein a biological activity of a protease is its catalytic activity in which a polypeptide is hydrolyzed.

As used herein equivalent, when referring to two sequences of nucleic acids, means that the two sequences in question encode the same sequence of amino acids or equivalent proteins. When equivalent is used in referring to two proteins or peptides, it means that the two proteins or peptides have substantially the same amino acid sequence with only amino acid substitutions (such as, but not limited to, conservative changes such as those set forth in Table 2, above) that do not substantially alter the activity or function of the protein or peptide. When equivalent refers to a property, the property does not need to be present to the same extent (*e.g.*, two peptides can exhibit different rates of the same type of enzymatic activity), but the activities are usually substantially the same. Complementary, when referring to two nucleotide sequences, means that the two sequences of nucleotides are capable of hybridizing, typically with less than 25%, 15% or 5% mismatches between opposed nucleotides. If necessary, the percentage of complementarity will be specified. Typically the two molecules are selected such that they will hybridize under conditions of high stringency.

As used herein, an agent that modulates the activity of a protein or expression of a gene or nucleic acid either decreases or increases or otherwise alters the activity of the protein or, in some manner, up- or down-regulates or otherwise alters expression of the nucleic acid in a cell.

As used herein, a "chimeric protein" or "fusion protein" protease refers to a polypeptide operatively-linked to a different polypeptide. A chimeric or fusion protein provided herein can include one or more proteases or a portion thereof, such as single chain protease domains thereof, and one or more other polypeptides for any one or more of a transcriptional/translational control signals, signal sequences, a tag for localization, a tag for purification, part of a domain of an immunoglobulin G, and/or a targeting agent. These chimeric or fusion proteins include those produced by recombinant means as fusion proteins, those produced by chemical means, such as by chemical coupling, through, for example, coupling to sulfhydryl groups, and those produced by any other method whereby at least one protease, or a portion thereof, is linked, directly or indirectly via linker(s) to another polypeptide.

As used herein, operatively-linked when referring to a fusion protein refers to a protease polypeptide and a non-protease polypeptide that are fused in-frame to one another. The non-protease polypeptide can be fused to the N-terminus or C-terminus of the protease polypeptide.

As used herein, a targeting agent, is any moiety, such as a protein or effective portion thereof, that provides specific binding of the conjugate to a cell surface receptor, which in some instances can internalize bound conjugates or portions thereof. A targeting agent also can be one that promotes or facilitates, for example, affinity isolation or purification of the conjugate; attachment of the conjugate to a surface; or detection of the conjugate or complexes containing the conjugate.

As used herein, an antibody conjugate refers to a conjugate in which the targeting agent is an antibody.

As used herein, derivative or analog of a molecule refers to a portion derived from or a modified version of the molecule.

As used herein, "disease or disorder" refers to a pathological condition in an organism resulting from cause or condition including, but not limited to, infections, acquired conditions, genetic conditions, and characterized by identifiable symptoms. Diseases and disorders of interest herein are those involving complement activation, including those mediated by complement activation and those in which complement activation plays a role in the etiology or pathology. Diseases and disorders also include those that are caused by the absence of a protein such as an immune deficiency, and of interest herein are those disorders where complement activation does not occur due to a deficiency in a complement protein.

As used herein, a complement-mediated disorder is any disorder in which any one or more of the complement proteins plays a role in the disease, either due to an absence or presence of the protein. A complement-mediated disorder is one that is due to a deficiency in a complement protein. A complement-mediated disorder also is one that is due to the presence of any one or more of the complement proteins and the continued activation of the complement pathway.

As used herein, "treating" a subject with a disease or condition means that the subject's symptoms are partially or totally alleviated, or remain static following

treatment. Hence treatment encompasses prophylaxis, therapy and/or cure. Prophylaxis refers to prevention of a potential disease and/or a prevention of worsening of symptoms or progression of a disease. Treatment also encompasses any pharmaceutical use of a modified interferon and compositions provided herein.

As used herein, a therapeutic agent, therapeutic regimen, radioprotectant, or chemotherapeutic mean conventional drugs and drug therapies, including vaccines, which are known to those skilled in the art. Radiotherapeutic agents are well known in the art.

As used herein, treatment means any manner in which the symptoms of a condition, disorder or disease are ameliorated or otherwise beneficially altered. Treatment also encompasses any pharmaceutical use of the compositions herein.

As used herein, amelioration of the symptoms of a particular disease or disorder by a treatment, such as by administration of a pharmaceutical composition or other therapeutic, refers to any lessening, whether permanent or temporary, lasting or transient, of the symptoms that can be attributed to or associated with administration of the composition or therapeutic.

As used herein, prevention or prophylaxis refers to methods in which the risk of developing disease or condition is reduced.

As used herein an effective amount of a compound or composition for treating a particular disease is an amount that is sufficient to ameliorate, or in some manner reduce the symptoms associated with the disease. Such amount can be administered as a single dosage or can be administered according to a regimen, whereby it is effective. The amount can cure the disease but, typically, is administered in order to ameliorate the symptoms of the disease. Typically, repeated administration is required to achieve a desired amelioration of symptoms.

As used herein, "therapeutically effective amount" or "therapeutically effective dose" refers to an agent, compound, material, or composition containing a compound that is at least sufficient to produce a therapeutic effect. An effective amount is the quantity of a therapeutic agent necessary for preventing, curing, ameliorating, arresting or partially arresting a symptom of a disease or disorder.

As used herein, administration of a non-complement protease, such as a modified non-complement protease, refers to any method in which the non-complement protease is contacted with its substrate. Administration can be effected *in vivo* or *ex vivo* or *in vitro*. For example, for *ex vivo* administration a body fluid, such as blood, is removed from a subject and contacted outside the body with the modified non-complement protease. For *in vivo* administration, the modified non-complement protease can be introduced into the body, such as by local, topical, systemic and/or other route of introduction. *In vitro* administration encompasses methods, such as cell culture methods.

As used herein, an anticoagulant is a drug that helps prevent the clotting (coagulation) of blood. These drugs tend to prevent new clots from forming or an existing clot from enlarging.

As used herein, unit dose form refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art.

As used herein, "patient" or "subject" to be treated includes humans and human or non-human animals. Mammals include; primates, such as humans, chimpanzees, gorillas and monkeys; domesticated animals, such as dogs, horses, cats, pigs, goats, cows; and rodents such as mice, rats, hamsters and gerbils.

As used herein, a combination refers to any association between two or among more items. The association can be spacial or refer to the use of the two or more items for a common purpose.

As used herein, a composition refers to any mixture of two or more products or compounds (e.g., agents, modulators, regulators, etc.). It can be a solution, a suspension, liquid, powder, a paste, aqueous or non-aqueous formulations or any combination thereof.

As used herein, an "article of manufacture" is a product that is made and sold. As used throughout this application, the term is intended to encompass modified protease polypeptides and nucleic acids contained in articles of packaging.

As used herein, fluid refers to any composition that can flow. Fluids thus encompass compositions that are in the form of semi-solids, pastes, solutions, aqueous mixtures, gels, lotions, creams and other such compositions.

As used herein, a "kit" refers to a packaged combination, optionally including reagents and other products and/or components for practicing methods using the elements of the combination. For example, kits containing a modified protease polypeptide or nucleic acid molecule provided herein and another item for a purpose including, but not limited to, administration, diagnosis, and assessment of a biological activity or property are provided. Kits optionally include instructions for use.

As used herein, a cellular extract refers to a preparation or fraction which is made from a lysed or disrupted cell.

As used herein, an agent is said to be randomly selected when the agent is chosen randomly without considering the specific sequences involved in the association of a protein alone or with its associated substrates, binding partners and/or other components. An example of randomly selected agents is the use of a chemical library or a peptide combinatorial library, or a growth broth of an organism or conditioned medium.

As used herein, a prodrug is a compound that, upon *in vivo* administration, is metabolized or otherwise converted to the biologically, pharmaceutically or therapeutically active form of the compound. To produce a prodrug, the pharmaceutically active compound is modified such that the active compound is regenerated by metabolic processes. The prodrug can be designed to alter the metabolic stability or the transport characteristics of a drug, to mask side effects or toxicity, to improve the flavor of a drug or to alter other characteristics or properties of a drug. By virtue of knowledge of pharmacodynamic processes and drug metabolism *in vivo*, those of skill in this art, once a pharmaceutically active compound is known, can design prodrugs of the compound (see, *e.g.*, Nogrady (1985) *Medicinal Chemistry A Biochemical Approach*, Oxford University Press, New York, pages 388-392).

As used herein, a peptidomimetic is a compound that mimics the conformation and certain stereochemical features of a biologically active form of a particular peptide. In general, peptidomimetics are designed to mimic certain desirable properties of a compound, but not the undesirable properties, such as flexibility, that lead to a loss of a biologically active conformation and bond

breakdown. Peptidomimetics can be prepared from biologically active compounds by replacing certain groups or bonds that contribute to the undesirable properties with bioisosteres. Bioisosteres are known to those of skill in the art. For example the methylene bioisostere CH2S has been used as an amide replacement in enkephalin analogs (see, e.g., Spatola (1983) pp. 267-357 in Chemistry and Biochemistry of Amino Acids, Peptides, and Proteins, Weinstein, Ed. volume 7, Marcel Dekker, New York). Morphine, which can be administered orally, is a compound that is a peptidomimetic of the peptide endorphin. For purposes herein, polypeptides in which one or more peptidic bonds that form the backbone of a polypeptide are replaced with bioisosteres are peptidomimetics.

As used herein, antibody includes antibody fragments, such as Fab fragments, which are composed of a light chain and the variable region of a heavy chain.

As used herein, a receptor refers to a molecule that has an affinity for a particular ligand. Receptors can be naturally-occurring or synthetic molecules. Receptors also can be referred to in the art as anti-ligands.

As used herein, primer refers to an oligonucleotide containing two or more deoxyribonucleotides or ribonucleotides, typically more than three, from which synthesis of a primer extension product can be initiated. Experimental conditions conducive to synthesis include the presence of nucleoside triphosphates and an agent for polymerization and extension, such as DNA polymerase, and a suitable buffer, temperature and pH.

As used herein, animal includes any animal, such as, but not limited to; primates including humans, gorillas and monkeys; rodents, such as mice and rats; fowl, such as chickens; ruminants, such as goats, cows, deer, sheep; ovine, such as pigs and other animals. Non-human animals exclude humans as the contemplated animal. The proteases provided herein are from any source, animal, plant, prokaryotic and fungal. Most proteases are of animal origin, including mammalian origin.

As used herein, genetic therapy or gene therapy involves the transfer of heterologous nucleic acid, such as DNA, into certain cells, target cells, of a mammal, particularly a human, with a disorder or condition for which such therapy is sought. The nucleic acid, such as DNA, is introduced into the selected target cells, such as

directly or in a vector or other delivery vehicle, in a manner such that the heterologous nucleic acid, such as DNA, is expressed and a therapeutic product encoded thereby is produced. Alternatively, the heterologous nucleic acid, such as DNA, can in some manner mediate expression of DNA that encodes the therapeutic product, or it can encode a product, such as a peptide or RNA that in some manner mediates, directly or indirectly, expression of a therapeutic product. Genetic therapy also can be used to deliver nucleic acid encoding a gene product that replaces a defective gene or supplements a gene product produced by the mammal or the cell in which it is introduced. The introduced nucleic acid can encode a therapeutic compound, such as a protease or modified protease, that is not normally produced in the mammalian host or that is not produced in therapeutically effective amounts or at a therapeutically useful time. The heterologous nucleic acid, such as DNA, encoding the therapeutic product can be modified prior to introduction into the cells of the afflicted host in order to enhance or otherwise alter the product or expression thereof. Genetic therapy also can involve delivery of an inhibitor or repressor or other modulator of gene expression.

As used herein, heterologous nucleic acid is nucleic acid that is not normally produced *in vivo* by the cell in which it is expressed or that is produced by the cell but is at a different locus or expressed differently or that mediates or encodes mediators that alter expression of endogenous nucleic acid, such as DNA, by affecting transcription, translation, or other regulatable biochemical processes. Heterologous nucleic acid is generally not endogenous to the cell into which it is introduced, but has been obtained from another cell or prepared synthetically. Heterologous nucleic acid can be endogenous, but is nucleic acid that is expressed from a different locus or altered in its expression. Generally, although not necessarily, such nucleic acid encodes RNA and proteins that are not normally produced by the cell or in the same way in the cell in which it is expressed. Heterologous nucleic acid, such as DNA, also can be referred to as foreign nucleic acid, such as DNA. Thus, heterologous nucleic acid or foreign nucleic acid includes a nucleic acid molecule not present in the exact orientation or position as the counterpart nucleic acid molecule, such as DNA, is

found in a genome. It also can refer to a nucleic acid molecule from another organism or species (*i.e.*, exogenous).

Any nucleic acid, such as DNA, that one of skill in the art would recognize or consider as heterologous or foreign to the cell in which the nucleic acid is expressed is herein encompassed by heterologous nucleic acid; heterologous nucleic acid includes exogenously added nucleic acid that also is expressed endogenously. Examples of heterologous nucleic acid include, but are not limited to, nucleic acid that encodes traceable marker proteins, such as a protein that confers drug resistance, nucleic acid that encodes therapeutically effective substances, such as anti-cancer agents, enzymes and hormones, and nucleic acid, such as DNA, that encodes other types of proteins, such as antibodies. Antibodies that are encoded by heterologous nucleic acid can be secreted or expressed on the surface of the cell in which the heterologous nucleic acid has been introduced.

As used herein, a therapeutically effective product for gene therapy is a product that is encoded by heterologous nucleic acid, typically DNA, that, upon introduction of the nucleic acid into a host, a product is expressed that ameliorates or eliminates the symptoms, manifestations of an inherited or acquired disease or that cures the disease. Also included are biologically active nucleic acid molecules, such as RNAi and antisense.

As used herein, a control refers to a sample that is substantially identical to the test sample, except that it is not treated with a test parameter, or, if it is a plasma sample, it can be from a normal volunteer not affected with the condition of interest. A control also can be an internal control.

As used herein, recitation that a polypeptide consists essentially of a recited sequence of amino acids means that only the recited portion, or a fragment thereof, of the full-length polypeptide is present. The polypeptide can optionally, and generally will, include additional amino acids from another source or can be inserted into another polypeptide. For example, for purposes herein, recitation that a polypeptide consists essentially of the protease domain means that the only portion of the polypeptide is a protease domain or a catalytically active portion thereof. The

polypeptide can optionally, and generally will, include additional non-protease derived sequences of amino acids.

As used herein, the abbreviations for any protective groups, amino acids and other compounds, are, unless indicated otherwise, in accord with their common usage, recognized abbreviations, or the IUPAC-IUB Commission on Biochemical Nomenclature (see, (1972) Biochem. 11:1726).

B. TARGET: COMPLEMENT

The complement system and its components are the target substrates for modified proteases as provided herein. The proteases are modified or selected or identified to cleave one or more components of the system and to thereby provide a way to modulate the activity of the system. Such proteases can serve as therapeutics or as candidate therapeutics to modulate the activity of the complement system.

The complement system is part of the immune system and plays a role in the elimination of invading foreign organisms and initiates inflammatory responses. There are over 30 soluble and cell-membrane proteins that are part of the complement system. These proteins function not only in the antibody-mediated immune response, but also in the innate immune response to recognize and kill pathogens such as bacteria, virus-infected cells, and parasites. Complement proteins are produced constitutively by macrophages and hepatocytes, and are present in the circulation as inactive molecules. Several complement proteins are pro-enzyme proteases (termed zymogens) that are themselves activated by proteolytic cleavage to become effector proteases that cut peptide bonds in other complement proteins to activate them in turn. Since each activated protease can activate many substrate molecules, the initial activation is rapidly amplified to produce millions of effector molecules (a cascade). The complement system constitutes an irreversible cascade of proteolytic events whose termination results in the formation of multiple effector molecules that stimulate inflammation, facilitate antigen phagocytosis, and lyse some cells directly, and, thus, can serve as a therapeutic point of intervention for treatment of a variety of disorders that share a common pathology or include this system in the etiology or pathology.

There are three distinct pathways through which complement can be activated on the pathogen surface: the classical pathway, the alternative pathway, and the lectin pathway. These pathways are distinct in that the components required for their initiation are different, but the pathways ultimately generate the same set of effector molecules (see, *e.g.*, Figure 1). Likewise, the early events of each pathway are governed by a similar mechanism of triggered-enzyme cascades in which inactive complement zymogens are cleaved to yield two fragments, the larger of which is an active serine protease. The active protease is retained at the pathogen surface so that the subsequent complement zymogen is cleaved and activated to continue the proteolytic cascade of complement activation. The second fragment generated upon zymogen cleavage is a smaller peptide fragment which can act as a soluble mediator of complement functioning as an opsonin or proinflammatory mediator.

1. Nomenclature

The complement pathway contains over 30 soluble mediators (see Table 3), some of which are generated from the cleavage of inactive protein zymogens to yield two fragments. Table 3 depicts exemplary native complement proteins and provides a description of their polypeptide sequence, including the location in the polypeptide of encoded complement fragments thereof. For example, SEQ ID NO: 315 encodes a C5 complement protein and also encodes a C5a fragment of a complement protein, encoded by residues 678-751 of C5, that exhibits complement activity upon its generation following cleavage of C5 by a C5 convertase. The native components of complement are designated by a C followed by a number such as C1, C2, etc... The numbering of the complement components is based on the order of their discovery rather than the order of the sequence of reactions within the complement cascade. As a result, the sequence of reactions of the complement cascades is C1, C4, C2, C3, C5, C6, C7, C8, and C9. Following activation, the products of the cleavage reactions are designated by adding lower case letters, the larger fragment generally being designated "b" and the smaller fragment as "a" (*i.e.* C4 is cleaved to generate C4b and C4a). In some instances C2a is designated as the larger cleavage product, although more generally C2b is considered the larger cleavage product. Consequently, the C3 convertase C3b2b is sometimes referred to as C3b2a. Inactive complement cleavage

products are designated with an "i" (*i.e.* iC3b). The protein zymogen components specific to the alternative pathway of complement are not designated by a C, but are rather designated by different capital letters such as Factor B, which upon cleavage becomes Bb or Ba. The two initiating protease zymogens of the lectin pathway are designated as MASP-1 and MASP-2.

Table 3: Complement Proteins

Entry Name	AC #	Gene Name	Amino acid length	Description	SEQ ID NO
C1QA_HUMAN	P02745	C1QA	245	Complement C1q subcomponent, A chain precursor	298
C1QB_HUMAN	P02746	C1QB	251	Complement C1q subcomponent, B chain precursor	299
C1QC_HUMAN	P02747	C1QG,C1QC	245	Complement C1q subcomponent, C chain precursor	300
C1R_HUMAN	P00736	C1R	705	Complement C1r subcomponent precursor (Complement component 1, r subcomponent) [Contains: Complement C1r subcomponent heavy chain (aa:18-463); Complement C1r subcomponent light chain (aa:464-705)]	301; 302
C1S_HUMAN	P09871	C1S	688	Complement C1s subcomponent precursor (C1 esterase) [Contains: Complement C1s subcomponent heavy chain (aa:16-437); Complement C1s subcomponent light chain (aa:438-688)]	303, 304
C4BB_HUMAN	P20851	C4BPB	252	C4b-binding protein beta chain precursor	305
C4BP_HUMAN	P04003	C4BPA C4BP	597	C4b-binding protein alpha chain precursor (C4bp) (Proline-rich protein) (PRP)	306
CFAI_HUMAN	P05156	IF	583	Complement factor I precursor (EC 3.4.21.45) (C3B/C4B inactivator) [Contains: Complement factor I heavy chain (aa:19-335); Complement factor I light chain (340-583)]	307, 308
CLUS_HUMAN	P10909	CLU	449	Clusterin precursor (Complement-associated protein SP-40,40) (Complement cytolysis inhibitor) (CLI) (NA1/NA2) (Apolipoprotein J) (Apo-J) (Testosterone-repressed prostate message 2) (TRPM-2) [Contains: Clusterin beta chain (ApoJalpha) (Complement cytolysis inhibitor a chain) (aa: 23-227); Clusterin alpha chain (ApoJbeta) (Complement cytolysis inhibitor b chain) (aa:228-449)]	309
CO2_HUMAN	P06681	C2	752	Complement C2 precursor (EC 3.4.21.43) (C3/C5 convertase)	310, 311
CO3_HUMAN	P01024	C3	1663	Complement C3 precursor [Contains: Complement C3 beta chain (aa:23-667); Complement C3 alpha chain (aa:672-1663); C3a anaphylatoxin (aa:672-748);.Complement C3b alpha' chain (aa:749-1663); Complement C3c fragment (aa:749-954); Complement C3dg fragment (aa:955-1303); Complement C3g fragment (aa:955-1001); Complement C3d fragment (aa:1002-1303); C3f fragment (aa:1304-1320)]	312
CO4_HUMAN	P01028	C4A and C4B	1744	Complement C4 precursor [Contains: Complement C4 beta chain (aa:20-675); Complement C4 alpha chain (aa:680-1446); C4a anaphylatoxin (680-756); C4b (aa:757-1446); Complement C4 gamma chain (aa:1454-1744)]	313
CO5_HUMAN	P01031	C5	1676	Complement C5 precursor [Contains: Complement C5 beta chain (aa:19-673); Complement C5 alpha chain (aa:678-1676); C5a anaphylatoxin (aa:678-751); Complement C5	314

Entry Name	AC #	Gene Name	Amino acid length	Description	SEQ ID NO
				alpha' chain (aa:752-1676)]	
CO6_HUMAN	P13671	C6	934	Complement component C6 precursor	315
CO7_HUMAN	P10643	C7	843	Complement component C7 precursor	316
CO8A_HUMAN	P07357	C8A	584	Complement component C8 alpha chain precursor (Complement component 8 alpha subunit)	317
CO8B_HUMAN	P07358	C8B	591	Complement component C8 beta chain precursor (Complement component 8 beta subunit)	318
CO8G_HUMAN	P07360	C8G	202	Complement component C8 gamma chain precursor	319
CO9_HUMAN	P02748	C9	559	Complement component C9 precursor [Contains: Complement component C9a (aa:22-265); Complement component C9b (aa:266-559)]	320
CR1_HUMAN	P17927	CR1, C3BR	2039	Complement receptor type 1 precursor (C3b/C4b receptor) (CD35 antigen)	321
CR2_HUMAN	P20023	CR2, C3DR	1033	Complement receptor type 2 precursor (Cr2) (Complement C3d receptor) (Epstein-Barr virus receptor) (EBV receptor) (CD21 antigen)	322
DAF_HUMAN	P08174	DAF, CD55, CR	381	Complement decay-accelerating factor precursor (CD55 antigen)	323
IC1_HUMAN	P05155	SERPING 1, C1IN, C1NH	500	Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh)	324
MASP1_HUMAN	P48740	MASP1, CRARF, CRARF1, PRSS5	699	Complement-activating component of Ra-reactive factor precursor (EC 3.4.21.-) (Ra-reactive factor serine protease p100) (RaRF) (Mannan-binding lectin serine protease 1) (Mannose-binding protein associated serine protease) (MASP-1) [Contains: Complement-activating component of Ra-reactive factor heavy chain (aa:20-448); Complement-activating component of Ra-reactive factor light chain (aa:449-699)]	325,326 (V1); 327, 328 (V2); 329, 330 (V3)
MASP2_HUMAN	O00187	MASP2	686	Mannan-binding lectin serine protease 2 precursor (EC 3.4.21.-) (Mannose-binding protein associated serine protease 2) (MASP-2) (MBL- associated serine protease 2) [Contains: Mannan-binding lectin serine protease 2 A chain (aa:16-444); Mannan-binding lectin serine protease 2 B chain (aa:445-686)]	331, 332 (V1); 333, 334 (V2)
MBL2_HUMAN	P11226	MBL2, MBL	248	Mannose-binding protein C precursor (MBP-C) (MBP1) (Mannan-binding protein) (Mannose-binding lectin)	335
MCP_HUMAN	P15529	MCP	392	Membrane cofactor protein precursor (CD46 antigen) (Trophoblast leukocyte common antigen) (TLX)	336
CFAB_HUMAN	P00751	BF	764	Complement factor B precursor (C3/C5 convertase) (Properdin factor B) (Glycine-rich beta glycoprotein) (GBG) (PBF2) [Contains: Complement factor B Ba fragment (aa:26-259); Complement factor B Bb fragment (aa:260-764)]	337, 338
CFAD_HUMAN	P00746	DF	253	Complement factor D precursor (C3 convertase activator) (Properdin factor D) (Adipsin)	339, 340
CFAH_HUMAN	P08603	CFH, HF, HF1	1231	Complement factor H precursor (H factor 1)	341, 342
PROP_HUMAN	P27918	PFC	469	Properdin precursor (Factor P)	343, 344
FCN2_HUMAN	Q15485	FCN2	313	Ficolin-2 (collagen/fibrinogen domain-containing protein 2; ficolin B; serum lectin p35; L-Ficolin	660
FCN1_HUMAN	O00602	FCN1	326	Ficolin-1 (collagen/fibrinogen domain-containing protein 1; Ficolin A; M-Ficolin)	661
FCN3_HUMAN	O75636	FCN3	299	Ficolin-3 (collagen/fibrinogen domain-contain 3; collagen/fibrinogen domain-containing lectin 3 p35; Hakata antigen; Factor-H)	662

2. Pathways of Complement Initiation

The pathways of complement are distinct in that they rely on different molecules and mechanisms for their initiation, but the pathways are similar in that

they converge to generate the same set of effector molecules. The convergence point of the C pathways is the cleavage of C3 by C3 convertase (a C3 activating enzyme). Convertase is a general name used for a complement enzyme that converts an inactive complement protein into an active one. For example, C3 convertase converts inactive C3 to active C3a and C3b. Different enzyme complexes have C3 convertase activity. For example, in the classical pathway C4b2b acts as a C3 convertase, whereas in the alternative pathway, C3bBb is a C3 convertase (see Table 4). Cleavage of C3 generates C3b, which acts as an opsonin and as the main effector molecule of the complement system for subsequent complement reactions, and C3a, which is a peptide mediator of inflammation. The addition of C3b to each C3 convertase forms a C5 convertase to generate C5a and C5b. C5a, like C3a, is a peptide mediator of inflammation. C5b mediates the "late" events of complement activation initiating the sequence of reactions culminating in the generation of the membrane attack complex (MAC). Although the three pathways produce different C3 and C5 convertases, all of the pathways produce the split products of C3 and C5 and form MAC.

Table 4:

Complement Cascades			
	Alternative Pathway	**Classical Pathway**	**Lectin Pathway**
Activators	Pathogen surface molecules LPS, teichoic acid, zymosan	antigen-bound IgM and IgG; non-immune molecules	Pathogens via recognition of carbohydrates on surface
C3 convertase	C3bBb	C4b2b	C4b2b
C5 convertase	C3bBb3b	C4b2b3b	C4b2b3b
MAC	C5678poly9	C5678poly9	C5678poly9
anaphylatoxins	C3a, C5a	C3a, C4a, C5a	C3a, C4a, C5a

a. Classical Pathway

C1q is the first component of the classical pathway of complement. C1q is a calcium-dependent binding protein associated with the collectin family of proteins due to an overall shared structural homology (Malhotra R *et al., Clin Exp Immunol.* 1994, 97(2):4-9; Holmskov *et al. Immunol Today.* 1994, 15(2):67-74). Mannose binding lectin (MBL), the first component of the lectin pathway, also is a member of the collectin family. Collectins are named because they contain a collagen-like and lectin domain. The amino-terminal collagen-like region of the collectin structure interacts with cell surface receptors and confers structural stability to the protein. The

carboxy-terminal regions of the collectin structure have a calcium-dependent lectin activity. The lectin domain mediates the interaction of the collectins with a wide variety of pathogens due to the recognition of carbohydrate moieties on the surface of pathogens. Collectins, often called pattern recognition molecules, generally function as opsonins to target pathogens for phagocytosis by immune cells. In contrast to conventional collectins, such as MBL, the carboxy-terminal globular recognition domain of C1q does not have lectin activity but can serve as a "charged" pattern recognition molecule due to marked differences in the electrostatic surface potential of its globular domains (Gaboriaud *et al. J. Biol. Chem.*, 2003, 278(47): 46974-46982).

C1q initiates the classical pathway of complement in two different ways. First, the classical pathway is activated by the interaction of C1q with immune complexes (*i.e.* antigen-antibody complexes or aggregated IgG or IgM antibody) thus linking the antibody-mediated humoral immune response with complement activation. When the Fab portion (the variable region) of IgM or IgG binds antigen, the conformation of the Fc (constant) region is altered, allowing C1q to bind. C1q must bind at least 2 Fc regions to be activated, so it takes two IgG molecules to activate C1q. Serum IgM is a pentamer of five IgM molecules with five Fc regions, so IgM activates complement most efficiently. IgA, IgE and IgD do not bind C1q and cannot activate complement. C1q, however, also is able to activate complement in the absence of antibody thereby functioning in the innate or immediate immune response to infection. Besides antibody, complement activation also is achieved by the interaction of C1q with non-immune molecules such as polyanions (bacterial lipopolysaccharides, DNA, and RNA), certain small polysaccharides, viral membranes, C reactive protein (CRP), serum amyloid P component (SAP), and bacterial, fungal and virus membrane components.

C1q is part of the C1 complex which contains a single C1q molecule bound to two molecules each of the zymogens C1r and C1s. Binding of more than one of the C1q globular domains to a target surface (such as aggregated antibody or a pathogen), causes a conformational change in the $(C1r:C1s)_2$ complex which results in the activation of the C1r protease to cleave C1s to generate an active serine protease.

Active C1s cleaves subsequent complement components C4 and C2 to generate C4b and C2b, which together form the C3 convertase of the classical pathway. The C3 convertase cleaves C3 into C3b, which covalently attaches to the pathogen surface and acts as an opsonin, and C3a, which stimulates inflammation. Some C3b molecules associate with C4b2b complexes yielding C4b2b3b which is the classical cascade C5 convertase. Table 5 summarizes the proteins involved in the classical pathway of complement.

Table 5:

Proteins of the Classical Pathway		
Native Component	**Active Form**	**Function of the Active Form**
C1 ($C1q:(C1r:C1s)_2$)	C1q	Binds directly to pathogen surfaces or indirectly to antibody bound to pathogens
	C1r	Cleaves C1s to an active protease
	C1s	Cleaves C4 and C2
C4	C4b	Binds to pathogen and acts as an opsonin; binds C2 for cleavage by C1s
	C4a	Peptide mediator of inflammation
C2	C2b	Active enzyme of classical pathway C3/C5 convertase; cleaves C3 and C5
	C2a	Precursor of vasoactive C2 kinin
C3	C3b	Binds to pathogen surfaces and acts as an opsonin; initiates amplification via the alternative pathway; binds C5 for cleavage by C2b
	C3a	Peptide mediator of inflammation

b. Alternative Pathway

The alternative pathway is initiated by foreign pathogens in the absence of antibody. Instead, the initiation of complement by the alternative pathway occurs through the spontaneous hydrolysis of C3 into C3b. A small amount of C3b is always present in body fluids, due to serum and tissue protease activity. Host self-cells normally contain high levels of membrane silica acid which inactivate C3b if it binds, but bacteria contain low external sialic acid and thereby bind C3b without inactivating

it. C3b on pathogen surfaces is recognized by the protease zymogen Factor B. Factor B is cleaved by Factor D. Factor D is the only activating protease of the C system that circulates as an active enzyme rather than as a zymogen, but since Factor B is the only substrate for Factor D the presence of low levels of an active protease in normal serum is generally safe for the host. Cleavage of Factor B by Factor D yields the active product Bb which can associate with C3b to form C3bBb, the C3 convertase of the alternative pathway. Similar to the classical pathway, the C3 convertase produces more C3b and C3a from C3. C3b covalently attaches to the pathogen surface and acts as an opsonin, while C3a stimulates inflammation. Some C3b joins the complex to form C3bBb3b, the alternative pathway C5 convertase. C3bBb3b is stabilized by the plasma protein properdin or Factor P which binds to microbial surfaces and stabilizes the convertase. Table 6 summarizes the proteins involved in the alternative pathway of complement.

Table 6:

Proteins of the Alternative Pathway		
Native Component	**Active Form**	**Function of the Active Form**
C3	C3b	Binds to pathogen surface, binds Factor B for cleavage by Factor D
Factor B	Ba	Small fragment of Factor B, unknown function
	Bb	Active enzyme of the C3 convertase and C5 convertase
Factor D	D	Plasma serine protease, cleaves Factor B when it is bound to C3b to Ba and Bb
Factor P (properdin)	P	Plasma proteins with affinity for C3bBb convertase on bacterial cells; stabilizes convertase

c. Lectin

The lectin pathway (also referred to as the MBL pathway) is initiated following recognition and binding of pathogen-associated molecular patterns (PAMPs; i.e. carbohydrates moieties) by lectin proteins. Examples of lectin proteins that activate the lectin pathway of complement include mannose binding lectin (MBL) and ficolins (*i.e.* L-ficolin, M-ficolin, and H-ficolin). As mentioned above, MBL is a member of the collectin family of proteins and thereby exists as an oligomer of subunits composed of identical polypeptide chains each of which contains a cysteine-

rich, a collagen-like, a neck, and a carbohydrate-recognition or lectin domain. MBL acts as a pattern recognition molecule to recognize carbohydrate moieties, particularly neutral sugars such as mannose or N-acetylglucosamine (GlcNAc) on the surface of pathogens via its globular lectin domain in a calcium-dependent manner. Besides a role in the complement system, MBL also acts as an opsonin to facilitate the phagocytosis of bacterial, viral, and fungal pathogens by phagocytic cells. In addition, other initiators of the lectin pathway include the ficolins including L-ficolin, M-ficolin, and H-ficolin (see e.g., Liu et al. (2005) J Immunol., 175:3150-6). Similar to MBL, ficolins recognize carbohydrate moieties such as, for example, N-acetyl glucosamine and mannose structures.

The activation of the alternative pathway by MBL or ficolins is analogous to activation of the classical pathway by C1q whereby a single lectin molecule interacts with two protease zymogens. In the case of the lectin proteins, the zymogens are MBL- associated serine proteases, MASP-1 and MASP-2, which are closely homologous to the C1r and C1s zymogens of the classical pathway. Upon recognition of a PAMP by a lectin protein, such as for example by binding to a pathogen surface, MASP-1 and MASP-2 are activated to cleave C4 and C2 to form the MBL cascade C3 convertase. C3b then joins the complex to form the MBL cascade C5 convertase. MASP activation is implicated not only in responses to microorganisms, but in any response that involves exposing neutral sugars, including but not limited to tissue injury, such as that observed in organ transplants. Like the alternative cascade, the MBL cascade is activated independent of antibody; like the classical cascade, the MBL cascade utilizes C4 and C2 to form C3 convertase. Table 7 summarizes the proteins involved in the lectin pathway of complement.

Table 7:

Proteins of the Lectin Pathway		
Native Component	**Active Form**	**Function of the Active Form**
MBL	MBL	Recognizes PAMPs, such as on pathogen surfaces (e.g., via recognition of carbohydrates)
Ficolins	L-Ficolin; M-Ficolin, or H-Ficolin	Recognizes PAMPs, such as on pathogen surfaces (e.g., via recognition of carbohydrates)

MASP-1	MASP-1	Cleaves C4 and C2
MASP-2	MASP-2	Cleaves C4 and C2

3. Complement-Mediated Effector functions

Regardless of which initiation pathway is used, the end result is the formation of activated fragments of complement proteins (*e.g.* C3a, C4a, and C5a anaphylatoxins and C5b-9 membrane attack complexes). These fragments mediate several functions including leukocyte chemotaxis, activation of macrophages, vascular permeability and cellular lysis (Frank, M. and Fries, L. Complement. In Paul, W. (ed.) Fundamental Immunology, Raven Press, 1989). A summary of some effector functions of complement products are listed in Table 8.

Table 8: Complement Effector Molecules and Functions

Product	Activity
C2b (prokinin)	accumulation of body fluid
C3a (anaphylatoxin)	basophil and mast cell degranulation; enhanced vascular permeability; smooth muscle contraction; Induction of suppressor T cells
C3b and its products	opsonization; Phagocyte activation
C4a (anaphylatoxin)	basophil & mast cell activation; smooth muscle contraction; enhanced vascular permeability
C4b	opsonization
C5a (anaphylatoxin; chemotactic factor)	basophil & mast cell activation; enhanced vascular permeability; smooth muscle contraction; chemotaxis; neutrophil aggregation; oxidative metabolism stimulation; stimulation of leukotriene release; induction of helper T-cells
C5b67	chemotaxis; attachment to other cell membranes and lysis of bystander cells
C5b6789 (C5b-9)	lysis of target cells

a. Complement-mediated lysis: Membrane Attack Complex

The final step of the complement cascade by all three pathways is the formation of the membrane attack complex (MAC) (Figure 1). C5 can be cleaved by any C5 convertase into C5a and C5b. C5b combines with C6 and C7 in solution, and the C5b67 complex associates with the pathogen lipid membrane via hydrophobic sites on C7. C8 and several molecules of C9, which also have hydrophobic sites, join to form the membrane attack complex, also called C5b6789 or C5b-9. C5b-9 forms a pore in the membrane through which water and solutes can pass, resulting in osmotic lysis and cell death. If complement is activated on an antigen without a lipid membrane to which the C5b67 can attach, the C5b67 complex can bind to nearby

cells and initiate bystander lysis. A single MAC can lyse an erythrocyte, but nucleated cells can endocytose MAC and repair the damage unless multiple MACs are present. Gram negative bacteria, with their exposed outer membrane and enveloped viruses, are generally susceptible to complement-mediated lysis. Less susceptible are Gram positive bacteria, whose plasma membrane is protected by their thick peptidoglycan layer, bacteria with a capsule or slime layer around their cell wall, or viruses which have no lipid envelope. Likewise, the MAC can be disrupted by proteins that bind to the complex before membrane insertion such as Streptococcal inhibitor of complement (SIC) and clusterin. Typically, the MAC helps to destroy gram-negative bacteria as well as human cells displaying foreign antigens (virus-infected cells, tumor cells, etc.) by causing their lysis and also can damage the envelope of enveloped viruses.

b. Inflammation

Inflammation is a process in which blood vessels dilate and become more permeable, thus enabling body defense cells and defense chemicals to leave the blood and enter the tissues. Complement activation results in the formation of several proinflammatory mediators such as C3a, C4a, and C5a. The intact anaphylatoxins in serum or plasma are quickly converted into the more stable, less active C3a-desArg, C4a-desArg, or C5a-desArg forms, by carboxypeptidase N. C3a, C4a and C5a, and to a lesser extent their desArg derivatives, are potent bioactive polypeptides, termed anaphylatoxins because of their inflammatory activity. Anaphylatoxins bind to receptors on various cell types to stimulate smooth muscle contraction, increase vascular permeability, and activate mast cells to release inflammatory mediators. Among the three anaphylatoxins, C5a is the most potent. C5a primarily acts on white blood cells, and in particular neutrophils. C5a stimulates leukocyte adherence to blood vessel walls at the site of infection by stimulating the increased expression of adhesion molecules so that leukocytes can squeeze out of the blood vessels and into the tissues, a process termed diapedesis. C5a also stimulates neutrophils to produce reactive oxygen species for extracellular killing, proteolytic enzymes, and leukotrienes. C5a also can further amplify the inflammatory process indirectly by inducing the production of chemokines, cytokines, and other proinflammatory

mediators. C5a also interacts with mast cells to release vasodilators such as histamine so that blood vessels become more permeable. C3a also interacts with white blood cells, with major effects on eosinophils suggesting a role for C3a in allergic inflammation. C3a induces smooth muscle contraction, enhances vascular permeability, and causes degranulation of basophils and release of histamine and other vasoactive substances. C2a can be converted to C2 kinin, which regulates blood pressure by causing blood vessels to dilate.

Although technically not considered an anaphylatoxin, iC3b, an inactive derivative of C3b, functions to induce leukocyte adhesion to the vascular endothelium and induce the production of the pro-inflammatory cytokine IL-1 via binding to its cell surface integrin receptors. C5b-9 also indirectly stimulates leukocyte adhesion, activation, and chemotaxis by inducing the expression of cell adhesion molecules such as E-selectin, and inducing interleukin-8 secretion (Bhole *et al.* (2003) *Crit Care Med* 31(1): 97-104). C5b-9 also stimulates the release of secondary mediators that contribute to inflammation, such as for example prostaglandin E_2, leukotriene B_4, and thromboxane.

Conversion of the human complement components C3 and C5 to yield their respective anaphylatoxin products has been implicated in certain naturally occurring pathologic states including: autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, malignancy, myocardial infarction, Purtscher's retinopathy, sepsis and adult respiratory distress syndrome. In addition, increased circulating levels of C3a and C5a have been detected in certain conditions associated with iatrogenic complement activation such as: cardiopulmonary bypass surgery, renal dialysis, and nylon fiber leukaphoresis. Elevated levels of C4a anaphylatoxin is associated with the autoimmune disorders mentioned above.

c. Chemotaxis

Chemotaxis is a process by which cells are directed to migrate in response to chemicals in their environment. In the immune response, a variety of chemokines direct the movement of cells, such as phagocytic cells, to sites of infection. For example, C5a is the main chemotactic factor for circulating neutrophils, but also can induce chemotaxis of monocytes. Phagocytes will move towards increasing

concentrations of C5a and subsequently attach, via their CR1 receptors, to the C3b molecules attached to the antigen. The chemotactic effect of C5a, observed with basophils, eosinophils, neutrophils, and mononuclear phagocytes, is active at concentrations as low as 10^{-10}M.

d. Opsonization

An important action of complement is to facilitate the uptake and destruction of pathogens by phagocytic cells. This occurs by a process termed opsonization whereby complement components bound to target bacteria interact with complement receptors on the surface of phagocytic cells such as neutrophils or macrophages. In this instance, the complement effector molecules are termed opsonins. Opsonization of pathogens is a major function of C3b and C4b. iC3b also functions as an opsonin. C3a and C5a increase the expression of C3b receptors on phagocytes and increase their metabolic activity.

C3b and, to a lesser extent, C4b help to remove harmful immune complexes from the body. The C3b and C4b attach the immune complexes to CR1 receptors on erythrocytes. The erythrocytes then deliver the complexes to fixed macrophages within the spleen and liver for destruction. Immune complexes can lead to a harmful Type III hypersensitivity

e. Activation of the Humoral Immune Response

Activation of B cells requires ligation of the B cell receptor (BCR) by antigen. It has been shown, however, that complement plays a role in lowering the threshold for B cell responses to antigen by up to 1000-fold. This occurs by the binding of C3d or C3dg, complement products generated from the breakdown fragments of C3, to CR2 receptors on B-lymphocytes which can co-ligate with the BCR. Co-ligation occurs when antigenic particles, such as for example immune complexes, opsonized with C3d binds the CR2 receptor via C3d as well as the BCR through antigen. Co-ligation of antigen complexes also can occur when C3d binds to antigens enhancing their uptake by antigen presenting cells, such as dendritic cells, which can then present the antigen to B cells to enhance the antibody response. Mice deficient in CR2 display defects in B cell function that result in reduced levels of natural antibody and impaired humoral immune responses.

4. Complement Receptors

The recognition of complement effector molecules by cells for the initiation of effector functions such as chemotaxis and opsonization is mediated by a diverse group of complement receptors. The complement receptors are distributed on a wide range of cell types including erythrocytes, macrophages, B cells, neutrophils, and mast cells. Upon binding of a complement component to the receptor, the receptors initiate an intracellular signaling cascade resulting in cell responses such as stimulating phagocytosis of bacteria and secreting inflammatory molecules from the cell. For example, the complement receptors CR1 and CR2 which recognize C3b, C4b, and their products are important for stimulating chemotaxis. CR3 (CD11b/CD18) and CR4 (CD11c/CD18) are integrins that are similarly important in phagocytic responses but also play a role in leukocyte adhesion and migration in response to iC3b. The C5a and C3a receptors are G protein-coupled receptors that play a role in many of the pro-inflammatory-mediated functions of the C5a and C3a anaphylatoxins. For example, receptors for C3a, C3aR, exist on mast cells, eosinophils, neutrophils, basophils and monocytes and are directly involved in the pro-inflammatory effects of C3a.

5. Complement Regulation

Although the complement system is beneficial to the host by protecting against foreign pathogens, the production of inflammatory mediators can be toxic and damaging leading to a wide variety of inflammatory disease conditions as discussed below. Likewise, although most of the active proteases of the complement system are zymogens that only become activated locally upon cleavage, nearly all components of complement are spontaneously activated at low rates in serum and thus their activity needs to be minimized. Consequently, regulatory proteins of the complement system have been identified. Their primary functions are to regulate the activity of complement activating molecules for prevention of excessive complement activation and autolytic destruction of host tissues. These complement regulators are either soluble plasma proteins or integral membrane proteins expressed on a variety of cell types. The former include C4b binding protein (C4bp) and Factor H. The latter include the C3b/C4b receptor (Complement receptor 1, CR1, CD35), membrane cofactor protein (MCP, CD46), and decay accelerating factor (DAF, CD55). These

proteins possess many structural similarities. Each is composed of multiple short consensus repeats (SCRs) of approximately 60 amino acids in length having conserved cysteine, glycine and proline residues. The genes encoding these proteins have been localized to chromosome 1 and are collectively known as the regulators of complement activation (RCA) gene cluster (Hourcade *et al.* (1989) *Adv. Immunol.* 45:381).

C1 inhibitor (C1INH) is a serine proteinase inhibitor or serpin which dissociates activated C1r and C1s from C1q, limiting the time the complex is active. C1INH also blocks spontaneous activation of C1 by plasma proteases. Deficiency in C1INH is associated with serious sudden edema (swelling) called Angioneurotic Edema. Several inhibitory proteins dissociate the C3 and C5 convertases and promote degradation of C4b and C3b by Factor I, a plasma protease. Factor I circulates in an active form but it is only able to cleave C3b and C4b when they are bound to a cofactor protein. Factor I cleaves C3b leading to the production of iC3b, C3c, C3d, C3f, and C3dg thereby permanently inactivating C3b, although the degradation products can act as effector molecules, since, for example, iC3b acts as an opsonin. C4b is inactivated upon cleavage into C4c and C4d. The inhibitory proteins that serve as cofactors for Factor I include plasma proteins C4 binding protein that dissociates classical C3 convertase, and Factor H that dissociates alternative C3 convertase, and membrane proteins Complement Receptor 1 (CR1), Decay Accelerating Factor (DAF), and Membrane Cofactor Protein (MCP) that inhibit the activity of both pathways. Cofactors for Factor I regulate its activity. For example, human cells produce Factor H that binds to C3b and allows Factor I to inactivate C3b. On the other hand, substances such as LPS on bacterial cells, which otherwise do not express Factor I cofactors, facilitate the binding of Factor B to C3b and this protects the C3b from inactivation by Factor I.

Other membrane and plasma proteins block the formation of MAC on host cells to prevent the inappropriate insertion of MAC into membranes. Several plasma proteins, such as the soluble protein C8β, bind to the C5b67 complex and inhibit its insertion into the cell membrane. Host cell membranes also contain a membrane-bound protein called HRF (CD59, protectin) which inhibits the binding of C9 to

C5b678 to prevent formation of the membrane attack complex on autologous or allogenic cells.

Factor I

Factor I (fI) is one of several serine proteases (also including factor D, MBL-associated serine protease (MASP)-2, C1s, C1r, factor B, and C2) of the complement system that play a role in the generation and amplification of the complement cascade reactions. All of the complement serine proteases share domain homology with the trypsin family and share some of the structural attributes that determine substrate specificity. The C-terminus of Factor I is made up of a trypsin-like serine protease light chain that, based on homology to other serine proteases, contains the residues that form the His-Asp-Ser catalytic triad. Additionally, residues are present that define the specificity pocket (D^{501}) and the extended substrate binding site S^{527}, W^{528}, and G^{529} (based on numbering of the mature protein in the absence of the signal peptide, see for example, Tsiftsoglou *et al.*, (2005) *Biochemistry* 44:6239).

Factor I plays a role in modulating complement activation by cleaving C3b and C4b, components of the C3 convertase in the classical, alternative, and lectin pathways thereby inactivating the pathways. Cleavage of fI substrates, C3b and C4b, requires a conformational change in the substrates caused by the formation of a thioester bond. For example, proteolytic activation of C3 to C3b by convertase results in a conformational change from the latent form to the C3b form which leads to reaction of an intramolecular thiolester with nucleophiles, such as water, thereby rendering C3b susceptible to fI cleavage (Ogata *et al.*, (1998) *J Immunol* 161:4785). Reaction of the thioester with water can occur in the absence of convertase cleavage, giving a hydrolyzed inactive form of C3 and C4 termed iC3 and iC4. For example, the iC3 species is a mimic of C3b; iC3 is sensitive to fI cleavage and can substitute for C3b in the C3 and C5 convertases. Generally, cleavage of the C3b and C4b substrates by Factor I requires the formation of a ternary complex with a cofactor protein, such as factor H or C4-binding protein, and MCP. Cleavage of synthetic substrates by Factor I, however, does not require the presence of cofactors (Tsiftsoglou *et al.*, (2004) *J Immunol* 173:367-375). Cleavage by fI is restricted to cleavage of arginyl bonds in the substrate. fI cleavage sites in C3 are LPSR (SEQ ID

NO: 388) and SLLR (SEQ ID NO: 389) and a cleavage site in C4 is HRGR (SEQ ID NO:390).

6. Complement-Mediated Diseases and Disorder

By virtue of the pivotal role of the complement system in the etiology of diseases and disorders, the system can serve as a point of therapeutic intervention in such diseases and disorders. The proteases provided herein target this system and permit modulation thereof.

The skilled artisan understands the role of the complement system in disease processes and is aware of a variety of such diseases. The following is a discussion of exemplary diseases and the role of the complement system in their etiology and pathology. Modulation of the complement system by the proteases provided herein can serve to treat such diseases. Diseases can involve complement activation or inhibition.

a. Disease mediated by Complement activation

The complement cascade is a dual-edged sword, causing protection against bacterial and viral invasion by promoting phagocytosis and inflammation. Conversely, even when complement is functioning normally, it can contribute to the development of disease by promoting local inflammation and damage to tissues. Thus, pathological effects are mediated by the same mediators that are responsible for the protective roles of complement. For example, the anaphylactic and chemotactic peptide C5a drives inflammation by recruiting and activating neutrophils, C3a can cause pathological activation of other phagocytes, and the membrane attack complex can kill or injure cells. In one example, such as in many autoimmune diseases, complement produces tissue damage because it is activated under inappropriate circumstances such as by antibody to host tissues. In other situations, complement can be activated normally, such as by septicemia, but still contributes to disease progression, such as in respiratory distress syndrome. Pathologically, complement can cause substantial damage to blood vessels (vasculitis), kidney basement membrane and attached endothelial and epithelial cells (nephritis), joint synovium (arthritis), and erythrocytes (hemolysis) if it is not adequately controlled.

Complement has a role in immuno-pathogenesis of a number of disorders, including autoimmune diseases such as rheumatoid arthritis (see, *e.g.*, Wang *et al.* (1995) *Proc. Natl. Acad. Sci.* U.S.A. 92:8955-8959; Moxley *et al.* (1987) *Arthritis & Rheumatism* 30:1097-1104), lupus erythematosus (Wang *et al.* (1996) *Proc. Natl. Acad. Sci.* U.S.A. 90:8563-8568; and Buyon *et al.* (1992) *Arthritis Rheum.* 35:1028-1037) and acute glomerulonephritis (Couser *et al.* (1995) *J Am Soc Nephrol.* 5:1888-1894). Other pathologies that involve activation of the complement system include sepsis (see, *e.g.*, Stove *et al.* (1996) *Clin Diag Lab Immunol* 3:175-183; Hack *et al.* (1989) *Am.J.Med.* 86:20-26), respiratory distress syndrome (see, *e.g.*, Zilow *et al.* (1990) *Clin.Exp.Immunol.* 79:151-157; and Stevens *et al.* (1986) *J.Clin.Invest.* 77:1812-1816), multiorgan failure (see, *e.g.*, Hecke *et al.* (1997) *Shock* 7:74; and Heideman *et al.* (1984) *J.Trauma* 24:1038-1043) and ischemia-reperfusion injury such as occurs in cardiovascular disease such as stroke or myocardial infarct (Austen WG *et al.* (2003) *Int J Immunopathol Pharm* 16(1):1-8). Some exemplary examples of complement-mediated disease are described below.

i. Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory illness. It is an autoimmune disease in which the immune system attacks normal tissue components as if they were invading pathogens. The inflammation associated with rheumatoid arthritis primarily attacks the linings of the joints. The membranes lining the blood vessels, heart, and lungs also can become inflamed. RA is characterized by activated B cells and plasma cells that are present in inflamed synovium, and in established disease lymphoid follicles and germinal centers. This results in high levels of local immunoglobulin production and the deposition of immune complexes, which can include IgG and IgM rheumatoid factors, in the synovium and in association with articular cartilage which can serve as initiators of the complement cascade. Elevated levels of complement components, such as C3a, C5a, and C5b-9 have been found within the inflamed rheumatoid joints. These complement components can exacerbate the inflammation associated with RA by inducing a variety of proinflammatory activities such as for example, alterations in vascular permeability, leukocyte chemotaxis, and the activation and lysis of multiple cell types.

ii. Sepsis

Sepsis is a disease caused by a serious infection, such as a bacterial infection, leading to a systemic inflammatory response. The bacterial cell wall component, lipopolysaccharide, is often associated with sepsis, although other bacterial, viral, and fungal infections can stimulate septic symptoms. Septic shock often results if the natural immune system of the body is unable to defend against an invading microorganism such that, for example, the pro-inflammatory consequences of the immune response is damaging to host tissues. The early stages of sepsis are characterized by excessive complement activation resulting in increased production of complement anaphylatoxins, such as C3a, C4a, and C5a which act to increase vascular permeability, stimulate superoxide production from neutrophils and stimulate histamine release. The actions of C5a can contribute to a productive immune response to a bacterial infection, but if left unregulated, C5a also can be severely damaging. In an *E.coli*-induced model of inflammation, blockade of C5a improved the outcome of septic animals by limiting C5a-mediated neutrophil activation that can lead to neutrophil-mediated tissue injury.

The continued impairment of the innate immune response to a bacterial infection often leads to chronic sepsis or septic shock, which can be life-threatening. In the late stage of sepsis, it is the "dormant" activity of neutrophils, as opposed to the hyperactivity that occurs in the early phases, that contributes to continued disease. In the late stage, the major functions of neutrophils including chemotaxis, respiratory burst activity, and ability for bacterial killing are reduced. Complement, and in particular C5a, also play a role in the later stages of sepsis. Excessive production of C5a during sepsis is associated with the "deactivation" of blood neutrophils, a process that has been linked to C5a-induced downregulation of its own receptor, C5aR, on neutrophils (Guo *et al.* (2003) *FASEB J* 13:1889). The reduced levels of C5aR on neutrophils correlates with a diminished ability of blood neutrophils to bind C5a, impaired chemotactic responses, a loss of superoxide productions, and impaired bactericidal activity. C5aR levels, however, can begin to "recover" at later stages of sepsis and correlate with instances of beneficial disease outcome.

iii. Multiple Sclerosis

Multiple sclerosis (MS) and its animal model experimental allergic encephalomyelitis (EAE) are inflammatory demyelinating diseases of the central nervous system (CNS). In MS, inflammation of nervous tissue causes the loss of myelin, a fatty material which acts as a sort of protective insulation for the nerve fibers in the brain and spinal cord. This demyelination leaves multiple areas of scar tissue (sclerosis) along the covering of the nerve cells, which disrupts the ability of the nerves to conduct electrical impulses to and from the brain, producing the various symptoms of MS. MS is mediated by activated lymphocytes, macrophages/microglia and the complement system. Complement activation can contribute to the pathogenesis of these diseases through its dual role: the ability of activated terminal complex C5b-9 to promote demyelination and the capacity of sublytic C5b-9 to protect oligodendrocytes (OLG) from apoptosis.

iv. Alzheimer's disease

Alzheimer's disease (AD) is characterized by tangles (abnormal paired helical filaments of the protein tau, which normally binds to microtubules) and plaques (extracellular deposits composed primarily of beta-amyloid protein) within the brain. Although, it is not entirely clear the what the precise cause of AD is, chronic neuroinflammation in affected regions of AD brains suggest that proinflammatory mediators can play a role. The tangles and plaques within an AD brain are deposited with activated complement fragments, such as for example, C4d and C3d. Likewise, dystrophic neurites in AD brain can be immunostained for MAC, indicating autocatalytic attack of these neurites and concomitant neurite loss in AD. Activation of complement in AD occurs by an antibody-independent mechanism induced by aggregated beta-amyloid protein. Further, the complement cascade can be activated by the pentraxins, C-reactive protein (CRP), and amyloid P (AP) which are all upregulated in AD (McGeer *et al.*, (2002) *Trends Mol Med* 8:519). The activation of complement in AD, marked by increases in complement mediators, is not adequately controlled by a compensatory upregulation of complement regulatory proteins such as, for example, CD59. Thus, the proinflammatory consequences of complement

activation exacerbates AD disease progression and likely contributes to neurite destruction.

v. Ischemia-Reperfusion Injury

Ischemia-reperfusion injury is the injury sustained after an ischemic event and subsequent restoration of blood flow and results from the inflammatory response to a hypoxic insult. Ischemia-reperfusion damage can be acute as during cardiac surgery procedures, such as for example following open heart surgery or angioplasty, or chronic as with congestive heart failure or occlusive cardiovascular disease. Examples of injuries that can cause ischemia-reperfusion injury include myocardial infarct (MI) and stroke. The initiation of an inflammatory response is likely caused by the increase in tissue oxygen levels that occur with reperfusion and the concomitant accumulation of metabolites that can generate oxygen free radicals which are immunostimulatory. It is associated with a variety of events including severity of myocardial infarction, cerebral ischemic events, intestinal ischemia, and many aspects of vascular surgery, cardiac surgery, trauma, and transplantation. The injury is manifested by inflammatory events of the innate immune system, particularly activation of the complement system, in response to newly altered tissue as non-self. As such ischemia-reperfusion injury is characterized by tissue edema caused by increased vascular permeability, and an acute inflammatory cell infiltrate caused by influx of polymorphonuclear leukocytes.

Activation of the complement system plays a role in the inflammatory events of ischemia-reperfusion injury. The ischemia injury results in alterations of the cell membrane, affecting lipids, carbohydrates, or proteins of the external surface such that these exposed epitopes are altered and can act as neo-antigens (modified self antigens). Circulating IgM recognize and bind the neo-antigens to form immune complexes on the injured cell surface. The antigen-antibody complexes formed are classic activators of the classical pathway of complement, although all pathways are likely involved in some way to the exacerbating effects of the injury. The involvement of the classical pathway of complement to ischemia-reperfusion injury is evidenced by mice genetically deficient in either C3 or C4 that display equal protection from local injury in a hindlimb and animal model of injury (Austen *et al.*

(2003) *Int J Immunopath Pharm* 16:1). Conversely, in a kidney model of ischemia injury, C3-, C5-, and C6-deficient mice were protected whereas C4-deficient mice were not, suggesting the importance of the alternative complement pathway (Guo *et al.* (2005) *Ann Rev Immunol* 23:821). Mediators induced upon complement activation initiate an inflammatory response directed at the cell membrane at the site of local injury.

A major effector mechanism of complement in ischemia-reperfusion injury is the influx and activation of neutrophils to the inflamed tissue by complement components, such as for example C5a. Activation of neutrophils results in increased production of reactive oxygen species and the release of lysosomal enzymes in local injured organs which ultimately results in apoptosis, necrosis, and a loss or organ function. The generation of the terminal MAC, C5b-9, also contributes to local tissue injury in ischemia-reperfusion injury.

b. Disease mediated by Complement deficiencies

The development of disease also can occur due to the absence of complement components that are important for controlling infection. Complement deficiencies are linked with frequent infections and immune complex diseases. Deficiencies have been identified in all of the complement factors except C9, including Factor D and properdin. Deficiencies also have been identified in the complement regulatory proteins C1INH, Factor I, Factor H, DAF, and HRF.

In general, deficiencies in complement components result in increased bacterial infections due to reduced opsonization and phagocytosis. Typically, deficiencies in complement components that function as opsonins, such as for example C3b, result in increased susceptibility to infection. For example, whereas individuals deficient in any of the late components of complement are relatively unaffected, individuals lacking C3 or any of the molecules that catalyze C3b deposition show increased susceptibility to infection by a wide range of extracellular bacteria. Likewise, people deficient in MBL, which normally functions as a traditional opsonin and as the initiator of the lectin pathway of complement following recognition of foreign pathogens, have increased susceptibility to infection, particularly during early childhood. The role of deficiencies in the late components of

complement, including C5-C9 that are involved in the formation of the membrane attack complex, to bacterial infection is more limited. Deficiencies in C5-C9 have only been shown to be associated with susceptibility to infection by *Neisseria* species, the bacteria that causes gonorrhea and bacterial meningitis.

Another consequence of complement deficiency is immune complex disease. Immune complex disease is caused by complement-mediated inflammation in response to persisting antigen-antibody complexes in the circulation and the tissues. Since the early components of the classical complement pathway initiate complement in response to the recognition of antigen-antibody complexes, deficiencies of these early components, such as for example C1q, can cause significant pathology in autoimmune disease such as systemic lupus erythematosus.

Deficiencies in complement regulatory proteins such as Factor H, DAF, and HRF also can result in complement-mediated disease. For example, uncontrolled complement activation can result in depletion of complement proteins resulting in an increased infection by bacteria, particularly ubiquitous pyogenic bacteria. This is the case in genetic factor I deficiency where factor I is not present and unable to inhibit the activation of the C3 convertase. Other examples include the complement regulatory proteins DAF or HRF, which normally function to protect a person's own cell surfaces from complement activation, but when deficient result in the destruction of host red blood cells resulting in the disease paroxysmal nocturnal hemoglobinuria. Deficiencies in C1-inhibitor causes the disease hereditary angioneurotic edema which is a result of the unregulated activity of serine proteinase enzymes including the complement components C1r and C1s, as well as other serine proteinases such as factor XIIa and kallikrein. The result of the unregulated activity of these serine proteinases is the production of a variety of vasoactive mediators, such as C2 kinin that is produced by the activity of C1s and C2a, resulting in fluid accumulation in the tissues and epiglottal swelling that can lead to suffocation.

C. PROTEASES

Provided herein are proteases and methods of using the proteases to cleave (thereby inactivating) proteins involved in disease processes. Typically, a protease provided herein is a non-complement protease that does not normally participate in

the complement pathways. Exemplary proteases provided herein cleave any one or more proteins or components of the complement pathway and allelic variants thereof. Cleavage of a complement protein can be an activating cleavage whereby the activity of the complement pathway is enhanced, such as by cleavage of a zymogen to an activated form of a protease or cleavage of a complement protein into its cleavage effector molecules. Cleavage of a complement protein also can be an inhibitory cleavage whereby the activity of the complement protein is diminished. Provided herein are proteases that cleave a complement protein in an inhibitory manner, thereby inhibiting complement activation of any one or more of the complement pathways. The proteases provided herein can be used for modulating complement activation. A protease provided herein can cleave any one or more complement proteins *in vitro* or *in vivo* thereby affecting complement activation *in vitro* or *in vivo*.

A protease can be any portion of a full-length protease as long as the portion of the protease retains proteolytic activity. For example, a protease can include only the protease domain of a polypeptide or any catalytically active portion thereof. The protease domain can include a single chain protease domain thereof and can be a fusion protein or a conjugate as long as the resulting fusion protein or conjugate retains proteolytic activity.

If a protease, or portion thereof, recognizes a substrate sequence within a target protein or proteins, such as for example a complement protein, (i) that would alter the function *i.e.* by inactivation of the target protein(s) upon catalysis of peptide bond hydrolysis, and (ii) the target proteins(s) is a point of molecular intervention for a particular disease or diseases, than the engineered protease has a therapeutic effect via a proteolysis-mediated inactivation event. Complement activities that can be altered include, but are not limited to, hemolysis of red blood cells and/or the generation of effector complement cleavage products such as but not limited to C3a, C3b, C4a, C5a, C5b-9, and Bb. Biological activities of complement can be altered *in vitro* or *in vivo*. Generally, a complement activity is altered by a protease at least 0.1, 0.5, 1, 2, 3, 4, 5, or 10 fold compared to the absence of a protease. Typically, a biological activity is altered 10, 20, 50, 100 or 1000 fold or more compared to the activity in the absence of the protease. For purposes herein with reference to

complement activity, a protease modulates complement activation or a complement-mediated activity.

A protease provided herein can be from any one or more of the serine, cysteine, aspartic, metallo-, or threonine classes or proteases. A protease can be tested to determine if it cleaves any one or more of the complement proteins and/or it can be used as a scaffold to make modifications in any one or more of the amino acid residues that modulates specificity towards a target substrate and/or modulates an activity of a target substrate. Exemplary classes of proteases and amino acid determinants that contribute to substrate specificity are described below.

1. Classes of Proteases

Proteases (also referred to as proteinases or peptidases) are protein-degrading enzymes that recognize sequences of amino acids or a polypeptide substrate within a target protein. Upon recognition of the substrate sequence of amino acids, proteases catalyze the hydrolysis or cleavage of a peptide bond within a target protein. Such hydrolysis of a target protein, depending on the location of the peptide bond within the context of the full-length sequence of the target sequence, can inactivate a target.

Proteases are classified based on the way they attack the protein, either exo- or endo- proteases. Proteinases or endopeptidases attack inside the protein to produce large peptides. Peptidases or exopeptidases attack ends or fragments of protein to produce small peptides and amino acids. The peptidases are classified on their action pattern: aminopeptidase cleaves amino acids from the amino end: carboxypeptidase cleaves amino acids from the carboxyl end, dipeptidyl peptidase cleaves two amino acids; dipeptidase splits a dipeptide, and tripeptidase cleaves an amino acid from a tripeptide. Most proteases are small from 21,000 to 45,000 Daltons. Many proteases are synthesized and secreted as inactive forms called zymogens and subsequently activated by proteolysis. This changes the architecture of the active site of the enzyme.

Several distinct types of catalytic mechanisms are used by proteases (Barret et al. (1994) *Meth. Enzymol.* 244:18-61; Barret et al. (1994) *Meth. Enzymol* 244:461-486; Barret et al. (1994) *Meth. Enzymol.* 248:105-120; Barret et al. (1994) *Meth. Enzymol.* 248:183-228). Based on their catalytic mechanism, the carboxypeptidases

are subdivided into serine-, metallo and cysteine- type carboxypeptidases and the endopeptidases are the serine-, cysteine-, aspartic-, threonine- and metalloendopeptidases. Serine peptidases have a serine residue involved in the active center, the aspartic have two aspartic acids in the catalytic center, cysteine-type peptidases have a cysteine residue, threonine-type peptidases have a threonine residue, and metallo-peptidases use a metal ion in the catalytic mechanism. Generally, proteases can be divided into classes based on their catalytic activity such that classes of proteases can include serine, cysteine, aspartic, threonine, or metallo-proteases. The catalytic activity of the proteases is required to cleave a target substrate. Hence, modification of a protease to alter the catalytic activity of a protease could affect (*i.e.* enhance specificity/ selectivity) the ability of a protease to cleave a substrate.

Each protease has a series of amino acids that lines the active site pocket and makes direct contact with the substrate. Crystallographic structures of peptidases show that the active site is commonly located in a groove on the surface of the molecule between adjacent structural domains, and the substrate specificity is dictated by the properties of binding sites arranged along the groove on one or both sides of the catalytic site that is responsible for hydrolysis of the scissile bond. Accordingly, the specificity of a peptidase is described by the ability of each subsite to accommodate a sidechain of a single amino acid residue. The sites are numbered from the catalytic site, S1, S2...Sn towards the N-terminus of the substrate, and S1', S2'...Sn' towards the C-terminus. The residues they accommodate are numbered P1, P2...Pn, and P1', P2'...Pn', respectively. The cleavage of a target protein is catalyzed between P1 and P1' where the amino acid residues from the N to C terminus of the polypeptide substrate are labeled (Pi, ..., P3, P2, P1, P1', P2', P3', ..., Pj) and their corresponding binding recognition pockets on the protease are labeled (Si,..., S3, S2, S1, S1', S2', S3',..., Sj) (Schecter and Berger (1967) *Biochem Biophys Res Commun* 27:157-162). Thus, P2 interacts with S2, P1 with S1, P1' with S1', *etc.* Consequently, the substrate specificity of a protease comes from the S1-S4 positions in the active site, where the protease is in contact with the P1-P4 residues of the peptide substrate sequences. In some cases, there is little (if any) interaction between the S1-S4 pockets of the active

site, such that each pocket appears to recognize and bind the corresponding residue on the peptide substrate sequence independent of the other pockets. Thus, the specificity determinants can be changed in one pocket without affecting the specificity of the other pocket.

Based upon numerous structures and modeling of family members, surface residues that contribute to extended substrate specificity and other secondary interactions with a substrate have been defined for many proteases including proteases of the serine, cysteine, aspartic, metallo-, and threonine families (see *e.g.* Wang et al., (2001) Biochemistry 40(34): 10038-46; Hopfner et al., (1999) Structure Fold Des. 7(8):989-96; Friedrich et al. (2002) J Biol Chem. 277(3):2160-8; Waugh et al., (2000) Nat Struct Biol. 7(9):762-5; Cameron *et al.*, (1993) *J Biol Chem.* 268:11711; Cameron *et al.*, (1994) *J Biol Chem.* 269: 11170). A protease can be tested to determine if it cleaves any one or more of the complement proteins and/or it can be used as a scaffold to make modifications in any one or more of the amino acid residues that modulates specificity towards a complement protein target substrate and/or modulates an activity of a complement protein target substrate. To make a modified protease with an altered substrate recognition profile, the amino acids in the three-dimensional structure that contribute to the substrate selectivity (specificity determinants) can be targeted for mutagenesis. Exemplary proteases include, but are not limited to, any protease such as a serine, cysteine, aspartic, metallo-, or threonine protease as described below and provided herein.

a. Serine Proteases

Serine proteases (SPs), which include secreted enzymes and enzymes sequestered in cytoplasmic storage organelles, have a variety of physiological roles, including roles in blood coagulation, wound healing, digestion, immune responses and tumor invasion and metastasis. For example, chymotrypsin, trypsin, and elastase function in the digestive tract; Factor 10, Factor 11, Thrombin, and Plasmin are involved in clotting and wound healing; and C1r, C1s, and the C3 convertases play a role in complement activation as discussed above.

A class of cell surface proteins designated type II transmembrane serine proteases are proteases which are membrane-anchored proteins with extracellular

domains. As cell surface proteins, they play a role in intracellular signal transduction and in mediating cell surface proteolytic events. Other serine proteases are membrane bound and function in a similar manner. Others are secreted. Many serine proteases exert their activity upon binding to cell surface receptors, and hence, act at cell surfaces. Cell surface proteolysis is a mechanism for the generation of biologically active proteins that mediate a variety of cellular functions.

Serine proteases, including secreted and transmembrane serine proteases, are involved in processes that include neoplastic development and progression. While the precise role of these proteases has not been fully elaborated, serine proteases and inhibitors thereof are involved in the control of many intra- and extracellular physiological processes, including degradative actions in cancer cell invasion and metastatic spread, and neovascularization of tumors that are involved in tumor progression. Proteases are involved in the degradation and remodeling of extracellular matrix (ECM) and contribute to tissue remodeling, and are necessary for cancer invasion and metastasis. The activity and/or expression of some proteases have been shown to correlate with tumor progression and development.

The activity of proteases in the serine protease family is dependent on a set of amino acid residues that form their active site. One of the residues is always a serine; hence their designation as serine proteases. For example, chymotrypsin, trypsin, and elastase share a similar structure and their active serine residue is at the same position (Ser-195) in all three. Despite their similarities, they have different substrate specificities; they cleave different peptide bonds during protein digestion. For example, chymotrypsin prefers an aromatic side chain on the residue whose carbonyl carbon is part of the peptide bond to be cleaved (R-group colored blue below). Trypsin prefers a positively charged Lys or Arg residue at this position. Serine proteases differ markedly in their substrate recognition properties: some are highly specific (*i.e.* the proteases involved in blood coagulation and the immune complement system); some are only partially specific (*i.e.* the mammalian digestive proteases trypsin and chymotrypsin); and others, like subtilisin, a bacterial protease, are completely non-specific. Despite these differences in specificity, the catalytic mechanism of serine proteases is well conserved.

The mechanism of cleavage of a target protein by a serine protease is based on nucleophilic attack of the targeted peptidic bond by a serine. Cysteine, threonine or water molecules associated with aspartate or metals also can play this role. In many cases the nucleophilic property of the group is improved by the presence of a histidine, held in a "proton acceptor state" by an aspartate. Aligned side chains of serine, histidine and aspartate build the catalytic triad common to most serine proteases. For example, the active site residues of chymotrypsin, and serine proteases that are members of the same family as chymotrypsin, such as for example MT-SP1, are Asp102, His57, and Ser195. Over 20 families (denoted S1-S27) of serine protease have been identified, these being grouped into 6 clans (SA, SB, SC, SE, SF and SG) on the basis of structural similarity and other functional evidence (Rawlings ND et al. (1994) *Meth. Enzymol.* 244: 19-61). There are similarities in the reaction mechanisms of several serine peptidases. Chymotrypsin, subtilisin and carboxypeptidase C clans have a catalytic triad of serine, aspartate and histidine in common: serine acts as a nucleophile, aspartate as an electrophile, and histidine as a base. The geometric orientations of the catalytic residues are similar between families, despite different protein folds. The linear arrangements of the catalytic residues commonly reflect clan relationships. For example the catalytic triad in the chymotrypsin clan (SA) is ordered HDS, but is ordered DHS in the subtilisin clan (SB) and SDH in the carboxypeptidase clan (SC).

Throughout the chymotrypsin family of serine proteases, the backbone interaction between the substrate and enzyme is completely conserved, but the side chain interactions vary considerably. The identity of the amino acids that contain the S1-S4 pockets of the active site determines the substrate specificity of that particular pocket. Grafting the amino acids of one serine protease to another of the same fold modifies the specificity of one to the other. Typically, the amino acids of the protease that contain the S1-S4 pockets are those that have side chains within 4 to 5 angstroms of the substrate. The interactions these amino acids have with the protease substrate are generally called "first shell" interactions because they directly contact the substrate. There, however, can be "second shell" and "third shell" interactions that ultimately position the first shell amino acids. First shell and second shell substrate

binding effects are determined primarily by loops between beta-barrel domains. Because these loops are not core elements of the protein, the integrity of the fold is maintained while loop variants with novel substrate specificities can be selected during the course of evolution to fulfill necessary metabolic or regulatory niches at the molecular level. Typically for serine proteases, the following amino acids in the primary sequence are determinants of specificity: 195, 102, 57 (the catalytic triad); 189, 190, 191, 192, and 226 (S1); 57, the loop between 58 and 64, and 99 (S2); 192, 217, 218 (S3); the loop between Cys168 and Cys180, 215, and 97 to 100 (S4); and 41 and 151 (S2'), based on chymotrypsin numbering, where an amino acid in an S1 position affects P1 specificity, an amino acid in an S2 position affects P2 specificity, an amino acid in the S3 position affects P3 specificity, and an amino acid in the S4 position affects P4 specificity. Position 189 in a serine protease is a residue buried at the bottom of the pocket that determines the S1 specificity. Structural determinants for various serine proteases are listed in Table 9 with numbering based on the to the numbering of mature chymotrypsin, with protease domains for each of the designated proteases aligned with that of the protease domain of chymotrypsin. The number underneath the Cys168-Cys182 and 60's loop column headings indicate the number of amino acids in the loop between the two amino acids and in the loop. The yes/no designation under the Cys191-Cys220 column headings indicates whether the disulfide bridge is present in the protease. These regions are variable within the family of chymotrypsin-like serine proteases and represent structural determinants in themselves. Modification of a protease to alter any one or more of the amino acids in the S1-S4 pocket affect the specificity or selectivity of a protease for a target substrate.

Table 9: The structural determinants for various serine proteases

Residues that Determine Specificity														
	S4					**S3**		**S2**			**S1**			
	171	**174**	**180**	**215**	**Cys168 Cys182**	**192**	**218**	**99**	**57**	**60's loop**	**189**	**190**	**226**	**Cys191 Cys220**
Granzyme B	Leu	Tyr	Glu	Tyr	14	Arg	Asn	Ile	His	6	Gly	Ser	Arg	No
Granzyme A	Asn	Val	Met	Phe	17	Asn	Leu	Arg	His	7	Asp	Ser	Gly	Yes
Granzyme M	Arg	Ser	Met	Phe	15	Lys	Arg	Leu	His	8	Ala	Pro	Pro	Yes

Cathepsin G	Phe	Ser	Gln	Tyr	13	Lys	Ser	Ile	His	6	Ala	Ala	Glu	No
MT-SP1	Leu	Gln	Met	Trp	13	Gln	Asp	Phe	His	16	Asp	Ser	Gly	Yes
Neutrophil elastase	-	-	-	Tyr	5	Phe	Gly	Leu	His	10	Gly	Val	Asp	Yes
Chymase	Phe	Arg	Gln	Tyr	12	Lys	Ser	Phe	His	6	Ser	Ala	Ala	No
Alpha-tryptase	Tyr	Ile	Met	Trp	22	Lys	Glu	Ile	His	9	Asp	Ser	Gly	Yes
Beta-tryptase(I)	Tyr	Ile	Met	Trp	22	Gln	Glu	Val	His	9	Asp	Ser	Gly	Yes
Beta-tryptase (II)	Tyr	Ile	Met	Trp	22	Lys	Glu	Thr	His	9	Asp	Ser	Gly	Yes
Chymo-trypsin	Trp	Arg	Met	Trp	13	Met	Ser	Val	His	7	Ser	Ser	Gly	Yes
Easter	Tyr	Ser	Gln	Phe	16	Arg	Thr	Gln	His	14	Asp	Ser	Gly	Yes
Collage-nase	Tyr	Ile	-	Phe	12	Asn	Ala	Ile	His	8	Gly	Thr	Asp	Yes
Factor Xa	Ser	Phe	Met	Trp	13	Gln	Glu	Tyr	His	8	Asp	Ala	Gly	Yes
Protein C	Met	asn	Met	Trp	13	Glu	Glu	Thr	His	8	Asp	Ala	Gly	Yes
Plasma kallikrein	Tyr	Gln	Met	Tyr	13	Arg	Pro	Phe	His	11	Asp	Ala	Ala	Yes
Plasmin	Glu	Arg	Glu	Trp	15	Gln	Leu	Thr	His	11	Asp	Ser	Gly	Yes
Trypsin	Tyr	Lys	Met	Trp	13	Gln	Tyr	Leu	His	6	Asp	Ser	Gly	Yes
Thrombin	Thr	Ile	Met	Trp	13	Glu	Glu	Leu	His	16	Asp	Ala	Gly	Yes
tPA	Leu	Thr	Met	Trp	15	Gln	Leu	Tyr	His	11	Asp	Ala	Gly	Yes
uPA	His	Ser	Met	Trp	15	Gln	Arg	His	His	11	Asp	Ser	Gly	yes

i. MT-SP1

Exemplary of the scaffold protease contemplated for use in modulating complement activation or as a scaffold for further modification to increase its activity in modulating the complement pathway is membrane-type serine protease MT-SP1 (also called matriptase, TADG-15, suppressor of tumorigenicity 14, ST14); see SEQ ID NOS: 1, 2 and GenBank Accession Nos: AF118224 and AAD42765; (1999) *J. Biol. Chem. 274*:18231-18236; U.S. Patent No. 5,792,616; see, also Takeuchi (1999) *Proc. Natl. Acad. Sci. U.S.A. 96*:11054-1161. The protein designated herein as an exemplary scaffold is a 855 amino acid MT-SP1 protease (see SEQ ID NOS: 1 and 2). The nucleic acid molecule whose sequence is set forth in SEQ ID NO:1 (see, also Genbank AF118224) encodes the 855 amino acid MT-SP1 (SEQ ID NO: 2, GenBank AAD42765).

It is multidomain proteinase with a C-terminal serine proteinase domain (Friedrich et al. (2002) J Biol Chem 277(3):2160). A 683 amino acid variant of the protease has been isolated, but this protein appears to be a truncated form or an ectodomain form.

MT-SP1 is highly expressed or active in prostate, breast, and colorectal cancers and it may play a role in the metastasis of breast and prostate cancer. MT-SP1 also is expressed in a variety of epithelial tissues with high levels of activity and/or expression in the human gastrointestinal tract and the prostate. Other species of MT-SP1 are known. For example, a mouse homolog of MT-SP1 has been identified and is called epithin.

MT-SP1 contains a transmembrane domain, two CUB domains, four LDLR repeats, and a serine protease domain (or peptidase S1 domain) between amino acids 615-854 (set forth as SEQ ID NOS:9 and 10), which is highly conserved among all members of the peptidase S1 family of serine proteases, such as for example with chymotrypsin (SEQ ID NOS:7 and 8). MT-SP1 is synthesized as a zymogen, and activated to double chain form by cleavage. In addition, the single chain proteolytic domain alone is catalytically active and functional.

MT-SP1 belongs to the peptidase S1 family of serine proteases (also referred to as the chymotrypsin family), which also includes chymotrypsin and trypsin. Generally, chymotrypsin family members share sequence and structural homology with chymotrypsin. MT-SP1 is numbered herein according to the numbering of mature chymotrypsin, with its protease domain aligned with that of the protease domain of chymotrypsin and its residues numbered accordingly. Based on chymotrypsin numbering, active site residues are Asp102, His57, and Ser195. The linear amino acid sequence can be aligned with that of chymotrypsin and numbered according to the β sheets of chymotrypsin. Insertions and deletions occur in the loops between the beta sheets, but throughout the structural family, the core sheets are conserved. The serine proteases interact with a substrate in a conserved beta sheet manner. Up to 6 conserved hydrogen bonds can occur between the substrate and enzyme. All serine proteases of the chymotrypsin family have a conserved region at their N-terminus of the protease domain that is necessary for catalytic activity (*i.e.* IIGG, VVGG, or IVGG, where the first amino acid in this quartet is numbered according to the chymotrypsin numbering and given the designation Ile16. This numbering does not reflect the length of the precursor sequence).

The substrate specificity of MT-SP1 in the protease domain has been mapped using a positional scanning synthetic combinatorial library and substrate phage display (Takeuchi *et al.* (2000) *J Biol Chem* 275: 26333). Cleavage residues in substrates recognized by MT-SP1 contain Arg/Lys at P4 and basic residues or Gln at P3, small residues at P2, Arg or Lys at P1, and Ala at P1'. Effective substrates contain Lys-Arg-Ser-Arg in the P4 to P1 sites, respectively. Generally, the substrate specificity for MT-SP1 reveals a trend whereby if P3 is basic, then P4 tends to be non-basic; and if P4 is basic, then P3 tends to be non-basic. Known substrates for MT-SP1, including, for example, proteinase-activated receptor-2 (PAR-2), single-chain uPA (sc-uPA), the proform of MT-SP1, and hepatocyte growth factor (HGF), conform to the cleavage sequence for MT-SP1 specific substrates.

MT-SP1 can cleave selected synthetic substrates as efficiently as trypsin, but exhibit a more restricted specificity for substrates than trypsin. The catalytic domain of MT-SP1 has the overall structural fold of a (chymo)trypsin-like serine protease, but displays unique properties such as a hydrophobic/acidic S2/S4 subsites and an exposed 60 loop. Similarly, MT-SP1 does not indiscriminately cleave peptide substrates at accessible Lys or Arg residues, but requires recognition of additional residues surrounding the scissile peptide bond. This requirement for an extended primary sequence highlights the specificity of MT-SP1 for its substrates. For example, although MT-SP1 cleaves proteinase activated receptor-2 (PAR-2) (displaying a P4 to P1 target sequence of Ser-Lys-Gly-Arg), the enzyme does not activate proteins closely related to this substrate such as PAR-1, PAR-3, and PAR-4 that do not display target sequences matching the extended MT-SP1 specificity near the scissile bond (see Friedrich *et al.* (2002) *J Biol Chem* 277: 2160).

The protease domain of MT-SP1 (see, *e.g,* SEQ ID NOS: 9 and 10) is composed of a pro-region and a catalytic domain. The catalytically active portion of the polypeptide begins after the autoactivation site at amino acid residue 611 of the mature protein (see, *e.g.,* SEQ ID NOS: 1 and 2 at RQAR followed by the residues VVGG). The S1 pocket of MT-SP1 and trypsin are similar with good complementarity for Lys as well as Arg P1 residues, thereby accounting for some similarities in substrate cleavage with trypsin. The accommodation of the P1-Lys

residues is mediated by Ser^{190} whose side chain provides an additional hydrogen bond acceptor to stabilize the buried α-ammonium group (see Friedrich *et al.* (2002) *J Biol Chem* 277: 2160). The S2 pocket is shaped to accommodate small to medium-sized hydrophobic side chains of P2 amino acids and generally accepts a broad range of amino acids at the P2 position. Upon substrate binding, the S2 sub-site is not rigid as evidenced by the rotation of the Phe^{99} benzyl group. Association of the substrate amino acids at positions P3 (for either Gln or basic residues) and P4 (for Arg or Lys residues) appears to be mediated by electrostatic interactions in the S3 and S4 pockets with the acidic side chains of Asp-217 and/or Asp-96 which could favorably pre-orient specific basic peptide substrates as they approach the enzyme active site cleft. The side chain of a P3 residue also is able to hydrogen bond the carboxamide group of Gln^{192} or alternatively, the P3 side chain can extend into the S4 sub-site to form a hydrogen bond with Phe^{97} thereby weakening the inter-main chain hydrogen bonds with Gly^{216}. In either conformation, a basic P3 side chain is able to interact favorably with the negative potential of the MT-SP1 S4 pocket. The mutual charge compensation and exclusion from the same S4 site explains the low probability of the simultaneous occurrence of Arg/Lys residues at P3 and P4 in good MT-SP1 substrates. Generally, the amino acid positions of MT-SP1 (based on chymotrypsin numbering) that contribute to extended specificity for substrate binding include: 146 and 151 (S1'); 189, 190, 191, 192, 216, 226 (S1); 57, 58, 59, 60, 61, 62, 63, 64, 99 (S2); 192, 217, 218, 146 (S3); 96, 97, 98, 99, 100, 168, 169, 170, 170A, 171, 172, 173, 174, 175, 176, 178. 179, 180, 215, 217, 224 (S4). Table 10 summarizes the residues in MT-SP1 for some of the amino acid positions important for specificity interactions with a targeted substrate. Typically, modification of an MT-SP1 protease to alter any one or more of the amino acids in the extended specificity binding pocket or other secondary sites of interaction affect the specificity or selectivity of a protease for a target substrate.

Table 10: Structural determinants for MT-SP1 substrate cleavage

Residues that Determine Specificity			
S4	S3	S2	S1

171	174	180	215	Cys168 Cys182	192	218	99	57	60's loop (58-64)	189	190	226	Cys191 Cys220
Leu	Gln	Met	Trp	13	Gln	Asp	Phe	His	16	Asp	Ser	Gly	yes

ii. Granzyme B

Granzyme B also is exemplary of the scaffold proteases contemplated for use in modulating complement activation or for further modification to increase its activity in modulating a complement pathway. Granzyme B is a serine protease (S1-type) necessary for target cell lysis in cell-mediated immune responses. Granzyme B is linked to an activation cascade of caspases (aspartate-specific cysteine proteases) responsible for apoptosis execution and cleaves caspase-3, caspase-7, caspase-9 and caspase-10 to give rise to active enzymes mediating apoptosis. Granzyme B (SEQ ID NO:3, GenBank #:M17016) encodes a 247 amino acid polypeptide (SEQ ID NO: 4, GenBank #:P10144). The precursor granzyme B polypeptide has a signal sequence and propeptide activation peptide at amino acids 1 to 20. The mature granzyme B protein is characterized by a peptidase S1 or protease domain at amino acids 21-245.

Granzyme B is a member of the family of chymotrypsin fold serine proteases, and has greater than 50% identity to other members of the granzyme family including granzymes C-G, cathepsin G, and rat mast cell protease II. The protein is a sandwich of two six stranded, anti-parallel beta-barrel domains connected by a short alpha-helix.

A substrate cleavage site of wildtype granzyme B has a consensus recognition site of I/V (P4)-E/Q/M (P3)-P/T (P2)-D (P1). These amino acids line the P1-P4 pocket of the substrate for recognition and cleavage by granzyme B. Generally granzyme B has a preference for cleaving after Asp in its consensus recognition.

The structural determinants for granzyme B substrate cleavage have been identified by the three-dimensional structure of rat granzyme B (SEQ ID NOS: 5 and 6) in complex with ecotin (IEPD), a macromolecular inhibitor with a substrate-like binding loop (Waugh *et al.*, (2000) *Nature Struct. Biol* 7:762). The catalytic triad is composed of Asp102, His57 and Ser195. The surface loops are numbered according to the additions and deletions compared to alpha-chymotrypsin and represent the most variable regions of this structural family. Other structural determinants of specificity

include Lys 41, Ile99, Arg192, Asn218, Tyr215, Tyr174, Leu172, Arg226, and Tyr151, by chymotrypsin numbering. The other members of the granzyme family of serine proteases share only two of these amino acids with granzyme B. They are Tyr215 and Leu172, two residues that vary very little across the entire structural family. This indicates that while the sequence identity of the granzymes is high, their substrate specificities are very different. The structural determinants for granzyme B substrate specificity are listed in Table 11 with chymotrypsin numbering. Typically, modification of a granzyme B protease to alter any one or more of the amino acids in the extended specificity binding pocket, or other secondary sites of interactions, affects the specificity or selectivity of a protease for a target substrate including a complement protein target substrate.

Table 11: Structural determinants for Granzyme B substrate cleavage

Residues that Determine Specificity													
S4					S3		S2			S1			
171	174	180	215	Cys^{168} Cys^{182}	192	218	99	57	60's loop	189	190	226	Cys^{191} Cys^{220}
Leu	Tyr	Glu	Tyr	14	Arg	Asn	Ile	His	6	Gly	Ser	Arg	no

The importance of granzyme B structural determinants to specificity has been profiled using a combinatorial substrate library to determine the effect of a mutation on extended specificity. Mutation of Ile99, Arg192, Asn218 and Tyr174 to the amino acid alanine have shown that Ile99 contributes to P2 specificity, Asn218 and Arg192 to P3 specificity, and Tyr174 to P4 specificity. Since the P1 specificity of a protease represents the majority of its specificity, the modifications do not destroy unique specificity of granzyme B towards P1 aspartic acid amino acids but modulate specificity in the extended P2 to P4 sites. For the P3 and P4 subsites, mutations at Tyr174, Arg192 and Asn218 did not significantly affect the specificity. Y174A increases the activity towards Leu at P4, but the rest of the amino acids continue to be poorly selected. R192A and N218A both broaden the specificity at P3. Instead of a strong preference for glutamic acid, Ala, Ser, Glu and Gln are introduced into a modified protease. The overall activity (k_{cat}/K_m) of the mutant is less than 10% below the wild-type activity toward an ideal wild-type substrate,

N-acetyl-Ile-Glu-Pro-Asp-AMC (7-amino-4-methylcoumarin) (Ac-IEPD-AMC). A greater effect is observed at the P2 subsite. In wildtype granzyme B, the preference is broad with a slight preference for Pro residues. I99A narrows the P2 specificity to Phe and Tyr residues. Phe narrows specificity by nearly 5 times over the average activity of other amino acids at this position. Within the chymotrypsin family of serine proteases, more than a dozen proteases have a small residue at this structural site, either an asparagine, serine, threonine, alanine or glycine. From this group, two proteases have been profiled using combinatorial substrate libraries, (plasma kallikrein and plasmin), and both show strong preferences towards Phe and Tyr. These two results suggest that any serine protease that is mutated to an Asn, Ser, Thr, Gly or Ala at position 99 will show the same hydrophobic specificity found in plasma kallikrein, plasmin and the I99A granzyme B mutant.

P2 specificity determinants can be expanded to the contrasting mutation and substrate preference. For example, nearly two dozen chymotrypsin-fold serine proteases have an aromatic amino acid at position 99. Four of these proteases have been profiled using combinatorial substrate libraries: human granzyme B, tissue type plasminogen activator, urokinase type plasminogen activator, and membrane type serine protease 1. All but granzyme B have a preference for serine, glycine and alanine amino acids at the substrate P2 position.

b. Cysteine Proteases

Cysteine proteases have a catalytic mechanism that involves a cysteine sulfhydryl group. Deprotonation of the cysteine sulfhydryl by an adjacent histidine residue is followed by nucleophilic attack of the cysteine on the peptide carbonyl carbon. A thioester linking the new carboxy-terminus to the cysteine thiol is an intermediate of the reaction (comparable to the acyl-enzyme intermediate of a serine protease). Cysteine proteases include papain, cathepsin, caspases, and calpains.

Papain-like cysteine proteases are a family of thiol dependent endo-peptidases related by structural similarity to papain. They form a two-domain protein with the domains labeled R and L (for right and left) and loops from both domains form a substrate recognition cleft. They have a catalytic triad made up of the amino acids Cys25, His159, and Asn175. Unlike serine proteases which recognize and proteolyze

a target peptide based on a beta-sheet conformation of the substrate, this family of proteases does not have well-defined pockets for substrate recognition. The main substrate recognition occurs at the P2 amino acid (compared to the P1 residue in serine proteases).

The substrate specificity of a number of cysteine proteases (human cathepsin L, V, K, S, F, B, papain, and cruzain) has been determined using a complete diverse positional scanning synthetic combinatorial library (PS-SCL). The complete library contains P1, P2, P3, and P4 tetrapeptide substrates in which one position is held fixed while the other three positions are randomized with equal molar mixtures of the 20 possible amino acids, giving a total diversity of ~160,000 tetrapeptide sequences.

Overall, P1 specificity is almost identical between the cathepsins, with Arg and Lys being strongly favored while small aliphatic amino acids are tolerated. Much of the selectivity is found in the P2 position, where the human cathepsins are strictly selective for hydrophobic amino acids. Interestingly, P2 specificity for hydrophobic residues is divided between aromatic amino acids such as Phe, Tyr, and Trp (cathepsin L, V), and bulkly aliphatic amino acids such as Val or Leu (cathepsin K, S, F). Compared to the P2 position, selectivity at the P3 position is significantly less stringent. Several of the proteases, however, have a distinct preference for proline (cathepsin V, S, and papain), leucine (cathepsin B), or arginine (cathepsin S, cruzain). The proteases show broad specificity at the P4 position, as no one amino acid is selected over others.

The S2 pocket is the most selective and best characterized of the protease substrate recognition sites. It is defined by the amino acids at the following spatial positions (papain numbering): 66, 67, 68, 133, 157, 160, and 205. Position 205 plays a role similar to position 189 in the serine proteases - a residue buried at the bottom of the pocket that determines the specificity. The other specificity determinants include the following amino acids (numbering according to papain): 61 and 66 (S3); 19, 20, and 158 (S1). The structural determinant for various cysteine proteases are listed in Table 12. Typically, modification of a cysteine protease, such as for example a papain protease, to alter any one or more of the amino acids in the extended specificity binding pocket or other secondary sites of interaction affect the specificity

or selectivity of a protease for a target substrate including a complement protein target substrate.

Table 12: The structural determinants for various cysteine proteases

	Residues that Determine Specificity												
	Active Site Residues			S3		S2					S1		
	25	159	175	61	66	66	133	157	160	205	19	20	158
Cathepsin L	Cys	His	Asn	Glu	Gly	Gly	Ala	Met	Gly	Ala	Gln	Gly	Asp
Cathepsin V	Cys	His	Asn	Gln	Gly	Gly	Ala	Leu	Gly	Ala	Gln	Lys	Asp
Cathepsin K	Cys	His	Asn	Asp	Gly	Gly	Ala	Leu	Ala	Leu	Gln	Gly	Asn
Cathepsin S	Cys	His	Asn	Lys	Gly	Gly	Gly	Val	Gly	Phe	Gln	Gly	Asn
Cathepsin F	Cys	His	Asn	Lys	Gly	Gly	Ala	Ile	Ala	Met	Gln	Gly	Asp
Cathepsin B	Cys	His	Asn	Asp	Gly	Gly	Ala	Gly	Ala	Glu	Gln	Gly	Gly
Papain	Cys	His	Asn	Tyr	Gly	Gly	Val	Val	Ala	Ser	Gln	Gly	Asp
Cruzain	Cys	His	Asn	Ser	Gly	Gly	Ala	Leu	Gly	Glu	Gln	Gly	Asp

c. Aspartic Proteases

Aspartate proteases include the digestive enzyme pepsin, some proteases found in lysosomes, the kidney enzyme renin, and the HIV-protease. Two aspartate residues participate in acid/base catalysis at the active site. In the initial reaction, one aspartate accepts a proton from an active site H_2O, which attacks the carbonyl carbon of the peptide linkage. Simultaneously, the other aspartate donates a proton to the oxygen of the peptide carbonyl group. They can exhibit a variety of specificities, but typically cleave between two hydrophobic amino acids. Well defined S4, S3, S2, S1, S1', S2', S3', and S4' subsite pockets for the amino acid side chains of the substrate are hallmarks for these enzymes (see *e.g.* Brinkworth *et al.*, (2001) *J Biol Chem* 276:38844).

Exemplary aspartic proteases include retroviral proteases, such as the human immunodeficiency virus, type 1 (HIV-1) PR, or the avian myeloblastosis/Rous sarcoma virus (AMV/RSV) PR (Cameron *et al.*, (1993) *J Biol Chem.* 268:11711). The PRs possess substrate binding pockets that contain at least seven subsites (S4-S3') which interact with 7 amino acids of the substrate (P4-P3') (Cameron *et al.*, (1993) *J Biol Chem.* 268:11711; Cameron *et al.*, (1994) *J Biol Chem.* 269: 11170). Residues that contribute to substrate specificity of the AMV/RSV PR include P62,

I42, M73, R105', H7', Q63, R10', D41, I64 (S4); H65, V104', R105', G106', Q63, R10', L35', D37', G39, D41, G66, I67, I108', R111 (S3); I42, I44, H65, M73, A100, A40, D41, I64, G66, I67', I108 (S2); H65, V104', R105', G106', S107', R10', L35', D37', D37, G39, G66, I67, I108' (S1); H65', V104, R105, G106, S107, R10, L35, D37, D37', G39', G66', I67', I108 (S1'), I42', I44', H65', M73', A100', V104', A40', D41', I64', G66', I67, I108' (S2'); and S38', H65', V104, R105, G106, Q63', R10, L35, G39', D41', I64', G66', I67', I108, R111' (S3'), where the amino acid residues in the second subunit of the dimer are indicated by a prime. Residues that contribute to substrate specificity of the HIV-1 PR include D30, V56, P81', R8', D29, I47 (S4); G48, T80', P81' V82', R8', L23', D25', G27, D29, G49, I50, I84', R87 (S3); D30, V32, G48, V56, L76, A28, D29, I47, G49, I50', I84 (S2); G48, T80', P81', V82', N83', R8', L23', D25', D25, G27, G49, I50, I84' (S1); G48', T80, P81, V82, N83, R8, L23, D25, D25', G27', G49', I50', I84 (S1'); D30', V32', G48', V56', L76', T80' (S2'); and R8, L23, G27', D29', I47', G49', I50', I84, R87' (S3'), where the amino acid residues in the second subunit of the dimer are indicated by a prime. Typically, modification of an aspartic protease, such as for example a retroviral protease, to alter any one or more of the amino acids in the extended specificity binding pocket, or other secondary sites of interaction, affects the specificity or selectivity of a protease for a target substrate including a complement protein target substrate.

d. Metalloproteases

Metalloproteases (also called Zinc proteases) include the digestive enzymes carboxypeptidases, various matrix metalloproteases (MMPs) that are secreted by cells, ADAMs (a disintegrin and metalloprotease domain), and lysosomal proteases. These enzymes, including ADAMs and MMPs have roles in embryonic development, cell growth and proliferation, inflammatory responses, wound repair, multiple sclerosis, arthritis, and cancer progression and metastasis (Manzetti *et al.*, (2003) *J of Computer-Aided Mol. Design,* 17: 551). Some MMPs (e.g., collagenase) are involved in degradation of the extracellular matrix during tissue remodeling. For example, many of these enzymes can cleave components of the basement membrane and extracellular matrix. Some MMPs have roles in cell signaling relating to their ability

to release cytokines or growth factors, such as TNFα, TGFβ, and interleukins, from the cell surface by cleavage of membrane-bound pre-proteins.

A zinc binding motif at the active site of a metalloprotease includes two histidine residues whose imidazole side-chains are ligands to the Zn^{++}. During catalysis, the Zn^{++} promotes nucleophilic attack on the carbonyl carbon by the oxygen atom of a water molecule at the active site. An active site base (a glutamate residue in carboxypeptidase) facilitates this reaction by extracting a proton from the attacking water molecule. Generally, these enzymes have a common zinc binding motif (HExxHxxGxxH) in their active site, and a conserved methionine turn following the active site. Mutation of any one of the histidines ablates catalytic activity. The active site specificity differs between metalloproteases to accommodate different peptide backbones of substrates around the scissile bond. A crucial molecular determinant of MMP substrate specificity is the side chain of the amino acid at the P1' position. Thus, the S1' subsite is important in determining the peptide bond preference for cleavage. For example, the small S1' pocket of MMP-1and MMP-7 promotes a preference for small hydrophobic residues while other MMPs have large S1' pockets (Overall *et al.*, (2002) *Mol Biotech* 22:51). The S2 position also is a molecular determinant of specificity. For example, between MMP-2 and MMP-9, the S2 sub-site is one of the few differences between the catalytic clefts of the MMPs where the presence of Glu^{412} in MMP-2 versus Asp^{410} in MMP-9 play important roles in altering substrate specificity. In fact, among the larger MMP family the Glu^{412} position is highly variable where it is occupied by acidic residues, large hydrophobic residues, and even glycine. In contrast, most of the residues surrounding the S2 subsite are strictly conserved among all MMPs (Chen *et al.*, (2003) *J Biol Chem* 278:17158). Other molecular determinants of specificity are described in Table 13 below (see *e.g.*, Manzetti *et al.*, (2003) *J Computer-Aided Mol Design* 17:551). Typically, modification of a metalloprotease, such as for example a MMP or ADAM protease, to alter any one or more of the amino acids in the extended specificity binding pocket, or other secondary sites of interaction, affect the specificity or selectivity of a protease for a target substrate including a complement protein target substrate.

Table 13: The structural determinants for various metalloproteases

	S4	S3	S2	S1	S1'	S2'	S3'	S4'
MMP-3	F210 F83	F210 A169	H166 H211	L164 V198 P221	V163	L164	L164	L222
ADAM9	F317 V318 H357	V318 M315	V318 H351 N356	M315 H357	I344 A313 N373	N373 T312	S374 F333	G310
ADAM10	P391 V332 W331	V332 P391 N387	V332 H392	L329 H392	L327 T379 A418	V326	N366	T421

e. **Threonine**

Threonine proteases include the proteasome hydrolase. The proteasome is a large barrel-shaped protein complex made up of alpha and beta subunits. The beta subunits supply the catalytic machinery found within the two central rings of the complex. Typically, the mechanism of catalysis of the catalytically active beta subunit involves a conserved N-terminal threonine at each active site. The beta subunits become activated when the N-terminus is cleaved off, making threonine the N-terminal residue such that catalytic threonines are exposed at the lumenal surface. Hydrolysis is initiated by attack of an amide bond by the hydroxyl nucleophile on the catalytic machinery. The structural determinants of specificity of the beta subunits of the proteasome have been determined, such as, for example by using libraries of peptide-based covalent inhibitors of the proteasome (see *e.g.*, Groll *et al.*, (2002) *Chem Biol* 9:655; Zhang *et al.*, (2003) *EMBO J*, 22:1488).

D. SCAFFOLD PROTEINS

Scaffold proteins are provided. Scaffold proteins include any wild-type protease so long as they are non-complement proteases, and also include allelic or species variants, or catalytically active portions thereof. The scaffold proteases can be used to target (i.e. cleave) any one or more complement pathway substrates. Typically, such cleavage results in inactivation of a complement pathway. In some instances, such cleavage can result in activation of complement. Hence, such scaffold proteases can be used as therapeutics by targeting complement pathway substrates to, for example, inhibit complement activation which is associated with the etiology of various diseases or disorders. Scaffold proteins also are any proteins that can be modified to cleave a target substrate. Among them are scaffold proteases, whose

target substrate specificity can be modified. Scaffold proteins, including proteases, can be modified in any one or more amino acids such that the resulting protease exhibits altered specificity or selectivity for any one or more protein components of the complement pathway and/or modulates an activity of a complement protein or pathway. For example, a modified protease can have an altered substrate specificity such that the modified protease preferentially cleaves a targeted substrate component of the complement pathway compared to a non-targeted substrate, such as for example a native substrate of a wildtype scaffold protease. In one embodiment, the specificity can be increased compared to the specificity of a wildtype or scaffold protease for a targeted substrate. In another example, a modified protease can exhibit a selectivity for a complement component such that the ability of a modified protease to cleave a particular substrate is greater than any other target substrate for which the modified protease also can exhibit specificity. Additionally, a modified protease can cleave a target substrate, such as for example any one or more proteins of a complement pathway, and modulate an activity of a complement pathway.

Exemplary scaffold proteases that can be used to cleave any one or more complement protein or can be used as a template to make modifications in the protease to increase substrate specificity or activity towards any one or more of the complement proteins are described. Protease scaffolds include any non-complement protease that is any one of the serine, cysteine, aspartic, metallo-, or threonine classes of proteases. Exemplary scaffold proteases are listed in Table 14 and described herein. Protease scaffolds include allelic variant and isoform of any one protein, including the scaffold protease polypeptides exemplified in any of SEQ ID NOS: 2, 4, 8, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 269, 270, 272, 274, 276, 278, 280, 282, 284, 286, 287, 289, 291, 293, 295, 297, 373, 375, 377, 379, 381, 383, 385, 387, 544, 545, 547, 549, and 551.

A scaffold protein or scaffold protease can be produced or isolated by any method known in the art including isolation from natural sources, isolation of recombinantly produced proteins in cells, tissues and organisms, and by recombinant methods and by methods including *in silico* steps, synthetic methods and any methods known to those of skill in the art. Table 14 sets forth exemplary scaffold proteases (see also *e.g.*, www.merops.sanger.ac.uk). The sequence identifiers (SEQ ID NO) for the nucleotide sequence and encoded amino acid precursor sequence for each of the exemplary candidate proteases is depicted in the Table. The encoded amino acids corresponding to the signal peptide or propeptide sequence to yield a mature protein also are noted in the Table. In addition, amino acids designating the protease domain (*i.e.* peptidase unit) also are noted, as are the active site residues that make up, for example, the catalytic triad of the respective protease. Since interactions are dynamic, amino acid positions noted are for reference and exemplification. The noted positions reflects a range of loci that vary by 2, 3, 4, 5 or more amino acids. Variations also exist among allelic variants and species variants. Those of skill in the art can identify corresponding sequences by visual comparison or other comparisons including readily available algorithms and software.

Table 14: Exemplary Scaffold Proteases

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
S01.010	granzyme B, human-type	GZMB	M17016	HLP, CCPI, CGL1, CSPB, SECT, CGL-1, CSP-B, CTLA1, CTSGL1	P10144	3, 4	1-18 / 19-20	21-247 (64, 108, 203)
S01.011	Testisin	PRSS21	NM_006799 (v1) NM_144956 (v2) NM_144957 (v3)	ESP-1, TEST1	NP_006790 NP_659205 NP_659206	70, 71 (V1); 72, 73 (V2); 74, 75 (V2)	1-19 / 20-41	42-288 (82, 137, 238)
S01.015	trypstase beta 1 (Homo sapiens) (III)	TPSB1	NM_003294	TPS1, TPS2, TPSAB1, alpha II	NP_003285	76, 77	1-18 / 19-30	31-274 (74, 121, 224)

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
S01.017	kallikrein hk5	KLK5	NM_012427	SCTE, KLKL2, KLK-L2	NP_036559	78, 79	1-22 /	67-292 (108, 153, 245)
S01.019	Corin		NM_006587	CRN, ATC2, Lrp4, TMPRSS10	NP_006578	80, 81		802-1037 (843, 892, 985)
S01.020	kallikrein 12	KLK12	NM_019598 (v1) NM_145894 (v2) NM_145895 (v3)	KLK-L5	NP_062544 NP_665901 NP_665902	82, 83 (V1); 84, 85 (V2); 86, 87 (V3)	1-17 /	22-248 (843, 892, 985)
S01.021	DESC1 oritease		AF064819		AAF04328	88, 89		191-422 (231, 276, 372)
S01.028	tryptase gamma 1	TPSG1	NM_012467	TMT, trpA, PRSS31	NP_036599	90, 91	1-19 /	38-272 (78, 125, 222)
S01.029	kallikrein hK14	KLK14	NM_022046	KLK-L6	NP_071329	92, 93	1-18 / 19-24	25-249 (67, 111, 204)
S01.033	hyaluronan-binding serine protease (HGF activator-like protein)	HABP2	NM_004132	FSAP, HABP, PHBP, HGFAL	NP_004123	94, 95	1-23 /	314-557 (362, 411, 509)
S01.034	transmembrane protease, serine 4	TMPRSS4	NM_019894 (v1) NM_183247 (v2)	MT-SP2, TMPRSS3	NP_063947 NP_899070	96, 97 (V1); 98, 99 (V2)		205-436 (245, 290, 387)
S01.054	tryptase delta 1 (Homo sapiens)	TPSD1	NM_012217	MCP7L1, MMCP-7L, MGC95428	NP_036349	100, 101	1-18 / 19-30	31-235 (74, 121, 224)
S01.074	Marapsin		NM_031948	PRSS27, CAPH2	NP_114154	102, 103	1-22 / 23-34	35-279 (75, 124, 229)
S01.075	Tryptase homologue 2 (Homo sapiens)		BC036846	PRSS33, EOS	AAN04055	104, 105		37-281 (77, 126, 231)
S01.076	Tryptase homologue 3 (Homo sapiens)		Putative Only AC005570 (Cosmid 407D8)			106, 107		67-304 (107, 213, 259)
S01.077	tryptase chromosome 21 (Homo sapiens)							
S01.079	transmembrane protease, serine 3	TMPRSS3	NM_024022 (vA) NM_032401 (vB) NM_032404 (vC) NM_032405 (vD)	DFNB8, DFNB10, ECHOS1, TADG12	NP_076927 NP_115777 NP_115780 NP_115781	108, 109 (VA); 110, 111 (vB); 112, 113 (vC); 114, 115 (vD)		217-451 (257, 304, 401)
S01.081	kallikrein hK15 (Homo		NM_023006 (v1) NM_13856	ACO, HSRNASPH	NP_075382 NP_61263	116, 117 (v1); 118, 119 (v2);	1-16 / 17-21	22-256 (62, 106, 209)

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
	sapiens)		3 (v2) NM_138564 (v3) NM_017509 (v4)		0 NP_612631 NP_059979	120, 121 (v3); 122, 123 (v4)		
S01.085	Mername-AA031 peptidase (deduced from ESTs by MEROPS)		BC035384	FLJ16649, MGC35022, TRYX3, UNQ2540	AAH35384	124, 125		1-241 (56, 101, 195)
S01.087	membrane-type mosaic serine protease		AB048796		BAB39741	126, 127		321-556 (361, 409, 506)
S01.088	mername-AA038 peptidase		Putative Only AL136097 (RP11-62C3 clone)		CAC12709	128		10-142 (50,101)
S01.098	mername-AA128 peptidase (deduced from ESTs by MEROPS)		Putative Only BC041609		AAH41609	129, 130		33-202 (50,152)
S01.127	cationic trypsin (Homo sapiens-type 1) (cationic)	PRSS1	NM_002769	TRP1, TRY1, TRY4, TRYP1	NP_002760	131, 132	1-15 / 16-23	24-246 (63, 107, 200)
S01.131	Neutrophils elastase	ELA2	NM_001972	NE, HLE, HNE, PMN-E	NP_001963	133, 134	1-27 / 28-29	30-249 (70, 117, 202)
S01.132	mannan-binding lectin-associated serine protease-3		AF284421		AAK84071	135, 136	1-19 /	449-710 (497, 553, 664)
S01.133	cathepsin G	CTSG	NM_001911	CG, MGC23078	NP_001902	137, 138	1-18 / 19-20	21-245 (64, 108, 201)
S01.134	myeloblastin (proteinase 3)	PRTN3	NM_002777	MBT, P29, ACPA, AGP7, PR-3, C-ANCA	NP_002768	139, 140	1-25 / 26-27	28-250 (71, 118, 203)
S01.135	granzyme A	GZMA	NM_006144	HFSP, CTLA3	NP_006135	141, 142	1-26 / 27-28	29-261 (69, 114, 212)
S01.139	granzyme M	GZMM	NM_005317	MET1, LMET1	NP_005308	143, 144	1-23 / 24-25	26-256 (66, 111, 207)
S01.140	chymase (human-type)	CMA1	NM_001836	CYH, MCT1	NP_001827	145, 146	1-19 / 21-21	22-247 (66, 110, 203)
S01.143	tryptase alpha (1)	TPS1	NM_003294	TPS1, TPS2, TPSB1, alpha II	NP_003285	147, 148	1-18 / 19-30	31-274 (74, 121, 224)

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
S01.146	granzyme K	GZMK	NM_002104	TRYP2	NP_002095	149, 150	1-24 / 26-26	27-261 (67, 116, 214)
S01.147	granzyme H	GZMH	NM_033423	CCP-X, CGL-2, CSP-C, CTLA1, CTSGL2	NP_219491	151, 152	1-18 / 19-20	21-246 (64, 108, 202)
S01.152	chymotrypsin B	CTRB1	M24400	CTRB, MGC88037	P17538	7, 8	1-18	34-263 (75, 120, 213)
S01.153	pancreatic elastase	ELA1	NM_001971		NP_001962	153, 154	1-8 / 9-18	19-256 (63, 111, 206)
S01.154	pancreatic endopeptidase E (A)		NM_005747	ELA3	NP_005738	155, 156	1-15 / 16-28	29-270 (73, 123, 217)
S01.155	pancreatic elastase II (IIA)		M16652		AAA52380	157, 158	1-16 / 7-28	29-269 (73, 121, 216)
S01.156	Enteropeptidase	PRSS7	NM_002772	ENTK	NP_002763	159, 160		785-1019 (825, 876, 971)
S01.157	chymotrypsin C		NM_007272	CLCR	NP_009203	161, 162	1-16 / 17-29	30-268 (74, 121, 216)
S01.159	Prostasin	PRSS8	NM_002773		NP_002764	163, 164	1-29 / 30-32	45-288 (85, 134, 238)
S01.160	kallikrein 1	KLK1	NM_002257	hK1, KLKR, Klk6	NP_002248	165, 166	1-18 / 19-24	25-261 (65, 120, 214)
S01.161	kallikrein hK2 (Homo sapiens)	KLK2	NM_005551 (v1) NM_001002231 (v2) NM_001002232 (v3)	hK2, KLK2A2, MGC12201	NP_005542 NP_001002231 NP_001002232	167, 168 (v1); 169, 170 (v2); 171, 172 (v3)	1-18 / 19-24	25-260 (65, 120, 213)
S01.162	kallikrein 3	KLK3	NM_001648 (v1) NM_001030047 (v3) NM_001030048 (v4) NM_001030049 (v5) NM_001030050 (v6)	APS, PSA, hK3, KLK2A1	NP_001639 NP_001025218 NP_001025219 NP_001025220 NP_001025221	173, 174 (v1); 175, 176 (v3); 177, 178 (v4); 179, 180 (v5); 181, 182 (v6)	1-17 / 18-24	25-260 (65, 120, 213)
S01.174	Mesotrypsin	PRSS3	NM_002771	MTG, TRY3, TRY4, PRSS4	NP_002762	183, 184	1-24 /	24-246 (63, 107, 200)
S01.205	pancreatic endopeptidase E form B (B)	ELA3B	NM_007352		NP_031378	185, 186	1-15 / 16-28	29-270 (73, 123, 217)
S01.206	pancreatic elastase II form B (Homos sapiens) (IIB)		NM_015849	MGC97052	NP_056933	187, 188	1-16 / 17-28	29-269 (73, 121, 216)
S01.211	coagulation factor XIIa	F12	NM_000505	HAF	NP_000496	189, 190	1-19 /	373-615 (412, 461, 563)
S01.212	plasma kallikrein	KLKB1	NM_000892	KLK3	NP_000883	191, 192	1-19 /	391-628 (434, 483, 578)
S01.213	coagulation	F11	NM_00012	FXI	NP_00011	193, 194	1-18 /	388-625

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
	factor XIa		8 (v1) NM_019559 (v2)		9 NP_062505	(v1); 195, 196 (v2)		(431, 480, 575)
S01.214	coagulation factor IXa	F9	NM_000133	FIX, PTC, HEMB, GLA domain	NP_000124	197, 198	1-28 / 29-46	227-461 (267, 315, 411)
S01.215	coagulation factor VIIa	F7	NM_000131 (v1) NM_019616 (v2)		NP_000122 NP_062562	199, 200 (v1); 201, 202 (v2)	1-20 / 21-60	213-454 (253, 302, 404)
S01.216	coagulation factor Xa	F10	NM_000504	FX, FXA	NP_000495	203, 204	1-31 / 32-40	235-469 (276, 322, 419)
S01.217	Thrombin	F2	NM_000506	PT	NP_000497	205, 206	1-24 / 25-43	364-620 (406, 462, 568)
S01.218	protein C (activated)	PROC	NM_000312	PROC1, protein C	NP_000303	207, 208	1-32 / 33-42	212-452 (253, 299, 402)
S01.223	Acrosin	ACR	NM_001097		NP_001088	209, 210	1-19	43-292 (88, 142, 240)
S01.224	Hepsin	HPN	NM_182983 (v1) NM_002151 (v2)	TMPRSS1	NP_892028 NP_002142	211, 212 (v1); 213, 214 (v2)		163-407 (203, 257, 353)
S01.228	hepatocyte growth factor activator	HGFAC	NM_001528	HGFA	NP_001519	215, 216	1-35 / 36-372	408-648 (447, 497, 598)
S01.231	u-plasminogen activator (uPA)	PLAU	NM_002658	ATF, UPA, URK, u-PA	NP_002649	217, 218	1-20 /	179-426 (224, 275, 376)
S01.232	t-plasminogen activator (tPA)	PLAT	NM_000930 (v1) NM_000931 (v2) NM_033011 (v3)	TPA, T-PA, DKFZp686I03148	NP_000921 NP_000922 NP_127509	219, 220 (v1); 221, 222 (V2), 223, 224 (V3)	1-23 / 24-32 and 33-35	311-562 (357, 406, 513)
S01.233	Plasmin	PLG	NM_000301	DKFZp779M0222	NP_000292	225, 226	1-19 / 20-97	581-810 (622, 665, 760)
S01.236	Neurosin	KLK6	NM_002774 (vA) NM_001012964 (vB) NM_001012965 (vC) NM_001012966 (vD)	hK6, Bssp, Klk7, SP59, ZYME, PRSS9, PRSS18, MGC9355, NEUROSIN	NP_002765 NP_001012982 NP_001012983 NP_001012984	227, 228 (vA); 229, 230 (vB); 231, 232 (vC); 233, 234 (vD)	1-16 / 17-21	22-244 (62, 106, 197)
S01.237	Neurotrypsin	PRSS12	NM_003619	BSSP3, BSSP-3, MGC12722, MOTOPSIN	NP_003610	235, 236	1-20 /	631-875 (676, 726, 825)
S01.242	tryptase beta 2 (Homo sapiens) (I)	TPSB1	NM_024164	TPS2, TPSB1, tryptaseC	NP_077078	237, 238	1-30 /	31-268
S01.244	Neuropsin	KLK8	NM_007196 (v1) NM_144505 (v2) NM_14450	NP, HNP, NRPN, PRSS19, TADG14	NP_009127 NP_653088 NP_65308	239, 240 (v1); 241, 242 (v2), 243, 244 (v3); 245,	1-28 / 29-32	33-258 (73, 120, 212)

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
			6 (v3) NM_144507 (v4)		9 NP_653090	246 (v4)		
S01.246	kallikrein hK10 (Homo sapiens)	KLK10	NM_002776 (v1) NM_145888 (v2)	NES1, PRSSL1	NP_002767 NP_665895	247, 248 (v1); 249, 250 (v2)	1-30 /	35-276 (86, 137, 229)
S01.247	Epitheliasin	TMPRSS2	NM_005656	PRSS10	NP_005647	251, 252		256-491 (296, 345, 441)
S01.251	Prostase	KLK4	NM_004917	ARM1, EMSP, PSTS, EMSP1, KLK-L1, PRSS17	NP_004908	253, 254	1-26 / 27-30	31-254 (71, 116, 207)
S01.252	Brain serine proteinase 2		NM_022119	BSSP-4, MGC9599, SP001LA, hBSSP-4	NP_071402	255, 256	1-32	50-292 (90, 141, 242)
S01.256	Chymopasin	CTRL	NM_001907	CTRL1, MGC70821	NP_001898	257, 258	1-18 / 19-33	34-264 (75, 121, 214)
S01.257	kallikrein 11	KLK11	NM_006853 (v1) NM_144947 (v2)	TLSP, PRSS20, MGC33060	NP_006844 NP_659196	259, 260 (v1); 261, 262 (v2)	1-50 /51-53	22-250 (62, 110, 203)
S01.258	anionic trypsin (Homo sapiens) (II)	PRSS2	NM_002770	TRY2, TRY8, TRYP2	NP_002761	263, 264	1-15 / 16-23	24-246 (63, 107, 200)
S01.291	LOC144757 peptidase (Homo sapiens)		Putative BC048112	MGC57341	AAH48112	265, 266		78-319 (122, 171, 268)
S01.292	Mername-AA169 peptidase		BN000133		CAD67985	267, 268	1-19	175-406 (215, 260, 356)
S01.294	Mername-AA171 peptidase		Putative No DNA			269		
S01.298	Mername-AA174 peptidase		Putative no DNA seq	TRY6	AAC80208	270		24-246 (63, 107, 200)
S01.299	Mername-AA175 peptidase		NM_198464		NP_940866	271, 272		68-302 (108, 156, 250)
S01.300	stratum corneum chymotryptic enzyme	KLK7	NM_005046 (v1) NM_139277 (v2)	SCCE, PRSS6	NP_005037 NP_644806	273, 274 (v1); 275, 276 (v2)	1-22 / 23-29	30-250 (70, 112, 205)
S01.301	trypsin-like enzyme, respiratory (Homo sapiens)		NM_004262	HAT	NP_004253	277, 278		187-471 (227, 272, 368)
S01.302	Matripase	ST14	AF118224	HAI, MTSP1, SNC19, MT-SP1, MTSP-1, PRSS14, TADG-15	AAD42765	1, 2		615-855 (656, 711, 805)
S01.306	kallikrein	KLK13	NM_01559	KLKL4,	NP_05641	279, 280	1-16 /	36-263

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
	hK13		6	KLK-L4, DKFZP586J1923	1			(76, 124, 218)
S01.307	kallikrein hK9 (human numbering)	KLK9	NM_012315	KLKL3, KLK-L3	NP_036447	281, 282	1-15 /	23-250 (63, 111, 204)
S01.308	Mername-AA035 peptidase		NM_153609		NP_705837	283, 284		49-283 (89, 140, 234)
S01.309	umbilical vein proteinase		NM_007173	SIG13, SPUVE, ZSIG13, MGC5107	NP_009104	285, 286	1-23 /	95-383 (175, 246, 316)
S01.311	LCLP proteinase (LCLP (N-terminus))		Peptide fragment No DNA		P34168	287		1-26 (0)
S01.313	Spinesin	TMPRSS5	NM_030770		NP_110397	288, 289		218-455 (258, 308, 405)
S01.318	Mername-AA178 peptidase	MPN2	NM_183062		NP_898885	290, 291	1-33 /	53-288 (93, 143, 238)
S01.320	Mername-AA180 peptidase	OVTN	BN000120		CAD66452	292, 293	1-23 /	52-301 (92, 142, 240)
S01.322	Mername-AA182 peptidase	OVCH1	BN000128		CAD67579	294, 295	1-17 /	8-298 (87, 139, 237)
S01.414	Mername-AA122 peptidase (deduced from ESTs by MEROPS)		Putative AK075142		BAC11431	296, 297		1-177 (12, 64, 168)
C01.032	Cathepsin L	CTSL	Y14734		P07711	372, 373	1-17 / 18-113	113-333 (132, 138, 276, 300)
C01.009	Cathepsin V	CTSL2	U13665		O60911	374, 375	1-17 / 18-113	114-334 (132, 138, 277, 301)
C01.036	Cathepsin K	CTSK	S93414		P43235	376, 377	1-15 / 16-114	115-329 (133, 139, 276, 296)
C01.034	Cathepsin S	CTSS	AJ007331		P25774	378, 379	1-16 / 17-114	115-331 (133, 139, 278, 298)
C01.018	Cathepsin F	CTSF	M14221		Q9UBX1	380, 381	1-19 / 20-270	271-484 (289, 295, 431, 451)
C01.060	Cathepsin B	CTSB	M15203		P07858	382, 383	1-17 / 18-79	80-331 (102, 108, 278, 298)
C01.001	Papain		M84342		P00784	384, 385	1-18 / 19-133	135-342 (158, 292, 308)
C01.075	Cruzain (Cruzapain)		Y14734		P25779	386, 387	123-467 /	124-334 (147, 284, 304,
A02.001	HIV-1 protease			HIV-1 retropepsin ; HIV-1 PR	P03366 (aa 500-598)	544		
A02.015	RSV			avian	P03322	545		

Merops Code	Name	Gene	Nucl. AC NO:	Synonym	Protein AC NO:	SEQ ID NO:	Signal/ Propep. sequence	Peptidase unit (active site residues)
	protease			myeloblastosis virus retropepsin; avian sarcoma virus endopeptidase; retropepsin	(aa 578-701)			
M10.005	Matrix metalloprotease-3	MMP3	X05232	collagenase activating protein; MMP-3; stromelysin 1; transin	CAA28859.1	546, 547		
M12.209	ADAM9 endopeptidase	ADAM9	NM_003816	MDC9	NP_003807	548, 549		
M12.210	ADAM10 endopeptidase	ADAM10	NM_003816	MADM	NP_001101	550, 551		

In some embodiments, the protease scaffold is a granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof. Such proteases can be used in the methods provided herein to target one or more target substrates of a complement pathway. Such proteases also can be modified to have altered specificity or selectivity for any one or more protein components of the complement pathway and/or to modulate an activity of a complement protein or pathway. The proteases or modified proteases can be used in the methods provided herein to modulate complement activation, and hence can be used as therapeutic to treat any complement-mediated disease or disorder. In some embodiments, the protease scaffold is MT-SP1. Modifications of amino acids in MT-SP1 can be made to alter the specificity and/or selectivity for a complement protein target substrate.

1. **Modified Scaffold Proteases**

Virtually every aspect of a protease can be re-engineered, including the enzyme substrate sequence specificity, thermostability, pH profile, catalytic efficiency, oxidative stability, and catalytic function. Provided herein are modified proteases that exhibit increased specificity and/or selectivity to any one or more complement proteins compared to a scaffold protease. Proteases can be modified using any method known in the art for modification of proteins. Such methods include site-directed and random mutagenesis. Assays such as the assays for biological function of complement activation provided herein and known in the art can be used to assess the biological function of a modified protease to determine if the modified protease targets a substrate for cleavage and inactivation. Exemplary methods to identify a protease and the modified proteases are provided herein.

For example, any of a variety of general approaches for protein-directed evolution based on mutagenesis can be employed. Any of these, alone or in combination can be used to modify a polypeptide such as a protease to achieve altered specificity and/or selectivity to a target substrate. Such methods include random mutagenesis, where the amino acids in the starting protein sequence are replaced by all (or a group) of the 20 amino acids either in single or multiple replacements at different amino acid positions on the same molecule, at the same time. Another method, restricted random mutagenesis, introduces either all or some of the 20 amino acids or DNA-biased residues. The bias is based on the sequence of the DNA and not on that of the protein in a stochastic or semi-stochastic manner, respectively, within restricted or predefined regions of the protein known in advance to be involved in the biological activity being "evolved." Exemplary methods for generating modified proteases are described in related U.S. application No. 10/677,977, herein incorporated by reference in its entirety. Additionally, any method known in the art can be used to modify or alter a protease polypeptide sequence.

Among the modified polypeptides provided herein are proteases with one or more modifications compared to a scaffold protease. Modified protease polypeptides include those with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more modified positions. Modified proteases provided herein retain their protease ability but display altered (*i.e.* enhanced) specificity towards any one or more

complement protein target substrates compared to a natural substrate of the protease and/or display an altered selectivity for any one or more proteins of the complement system. A modified protease specific for any one or more of the complement proteins can be generated rationally or empirically by: (a) rationally targeting sites that complement a cleavage sequence of a target complement substrate recognized by a known protease, such as for example, complement Factor I or, (b) empirically testing a library of modified proteases in functional assays for inactivation of the complement cascade.

a. Rational Modification

Methods are provided to rationally modify a protease to increase the specificity and/or selectivity to a target substrate, such as to any one or more complement proteins. In such a method, a cleavage sequence of the target substrate is known. Cleavage sites within target proteins are identified by the following criteria: 1) they are located on the exposed surface of the protein; 2) they are located in regions that are devoid of secondary structure (*i.e.* not in P sheets or helices), as determined by atomic structure or structure prediction algorithms (these regions tend to be loops on the surface of proteins or stalk on cell surface receptors); 3) they are located at sites that are likely to inactivate the protein, based on its known function. Cleavage sequences are *e.g.,* four residues in length to match the extended substrate specificity of many proteases, but can be longer or shorter.

Factor I is a serine protease that functions as a natural regulator of complement activation by cleaving C3b and C4b. Factor I cleaves and inactivates C3b and C4b after activation by the convertase on C3 and C4, respectively, and release of C3a and C4a. The peptide cleavage sequences recognized by Factor I include LPSR (SEQ ID NO: 388) and SLLR (SEQ ID NO: 389) in C3 and HRGR (SEQ ID NO: 390) in C4 (see *e.g.,* Davis *et al.,* (1982) *Biochemistry* 21:5745); Harrison *et al.,* (1980) *Mol. Immunology* 17:9; Kai *et al.,* (1980) *J Immunol.* 125:2409). Provided herein are methods to rationally design the specificity binding pocket of a protease to recognize and specifically cleave Factor I substrates, including C3 and C4 as well as iC3, C3b, iC4, and C4b, thereby inhibiting complement activation. Products that cleave the Factor I substrates are provided.

As an example, modified proteases with altered specificity for a Factor I target sequence are generated by a structure-based design approach. Each protease has a series of amino acids that line the active site pocket and make direct contact with a substrate. The amino acids that line the active site pocket of a protease are designated S1-S4 and the respective substrate contact sites are designated P1-P4. The identity of the amino acids that contain the S1-S4 pocket of the active site determines the substrate specificity of that particular pocket. Amino acids that form the substrate binding pocket of exemplary proteases are described herein. Generally, the substrate specificity of a protease is known or can be determined, such as, for example by molecular modeling based on three-dimensional structures of the complex of a protease and substrate (see for example, Wang *et al.*, (2001) *Biochemistry* 40(34):10038; Hopfner *et al.*, *Structure Fold Des.* 1999 7(8):989; Friedrich *et al.*, (2002) *J Biol Chem* 277(3):2160; Waugh *et al.*, (2000) *Nat Struct Biol.* 7(9):762). In one example, the amino acids that participate in the S1-S4 substrate binding pocket of MT-SP1 are as follows (based on chymotrypsin numbering): 189, 190, 191, 192, 216 and 226 (S1); 57, 58, 59, 60, 61, 62, 63, 64, 99 (S2); 146, 192, 217, 218 (S3); 96, 97, 98, 99, 100, 168, 169, 170, 170A, 171, 172, 173, 174, 175, 176, 178, 179, 180, 215, 217, 224 (S4). In another example, the amino acids in a papain family protease that contribute to P2 specificity (standard papain numbering) include amino acids 66-68, 133, 157, 160, and/or 215. Modifying any one or more of the amino acids that make up the S1-S4 active site of a protease would alter the substrate specificity of that protease. For example, a mutation at position 99 in the S2 pocket of a serine protease, such as for example an MT-SP1 protease, to a smaller amino acid confers a preference for larger hydrophobic residues in the P2 substrate position. Using this process of selective mutagenesis, proteases with substrate specificities to a Factor I cleavage sequence can be generated.

In one embodiment, point mutations can be made in the amino acids that contribute to the specificity binding pocket of a protease, particularly in any one or more S1-S4 amino acid residues that contribute to P1-P4 substrate specificity. Generally, the amino acid residues that contribute to the P1-P4 specificity of a protease can be rationally replaced so that the target substrate cleavage site recognized

by Factor I is produced. In one example, a protease can be modified to recognize the target cleavage sequence LPSR/KI where any one or more amino acids in the S4 position can be modified to recognize a leucine at the P4 position, any one or more amino acids in the S3 position can be modified to recognize a proline at the P3 position, any one or more amino acids in the S2 position can be modified to recognize a serine at the P2 position, and any one or more amino acids in the S1 position can be modified to recognize an arginine at the P1 position. In another example, a protease can be modified to recognize the target cleavage sequence SLLR/SE where any one or more amino acids in the S4 position can be modified to recognize a serine at the P4 position, any one or more amino acids in the S3 position can be modified to recognize a leucine at the P3 position, any one or more amino acids in the S2 position can be modified to recognize a leucine at the P2 position, and any one or more amino acids in the S1 position can be modified to recognize an arginine at the P1 position. In an additional example, a protease can be modified to recognize the target cleavage sequence HRGR/TL where any one or more amino acids in the S4 position can be modified to recognize a histidine at the P4 position, any one or more amino acids in the S3 position can be modified to recognize an arginine at the P3 position, any one or more amino acids in the S2 position can be modified to recognize a glycine at the P2 position, and any one or more amino acids in the S1 position can be modified to recognize an arginine at the P1 position. In some cases, mutations in serine proteases have shown that each of the sub-sites that form the active site (S1-S4) function independently of one another, such that modification of specificity at one sub-site has little influence on specificity at adjacent sub-sites. Thus, engineering substrate specificity and/or selectivity throughout the extended binding site can be accomplished in a step-wise manner.

For example, a protease with low specificity for a residue at a particular binding site or for a particular sequence is altered in its specificity by making point mutations in the substrate sequence binding pocket. In some cases, the resulting mutant has a greater than 1.5, 2, 5, 8, 10-fold or greater increase in specificity at a site for a particular sequence than does wildtype. In another embodiment, the resulting mutant has a greater than 100-fold increase in specificity at a site for a particular

sequence than does wildtype. In another embodiment, the resulting mutant has an over 1000-fold increase in specificity at a site or for a particular sequence than does a wildtype.

In one exemplary embodiment, wildtype MT-SP1 protease having a P1-P4 preference for a target cleavage sequence of Arg/Lys at P4, basic residues or Gln at P3, small residues at P2, and Arg or Lys at P1 can be modified so that the Factor I cleavage sequence of LPSR, SLLR, or HRGR is recognized by an MT-SP1 protease (see Table 15). In such an example, the S1 position of the modified MT-SP1 is unchanged since the arginine residue at the P1 site is conserved between the target substrate cleavage site of MT-SP1 and the Factor I cleavage sites. Amino acid residues in any one of more of the S2-S4 sub-sites of MT-SP1 can be modified alone or in combination to increase the specificity and/or selectivity for a Factor I cleavage sequence. For example, to modify an MT-SP1 set forth in SEQ ID NO:2 or 10 to have increased specificity and/or selectivity for a SLLR Factor I cleavage sequence in C3b, modifications in the S4 position of MT-SP1 to recognize a serine in the P4 position of the substrate can include amino acid modifications Q174H, D217Q, D217N, D217H, D96A, D96V, D96F, D96S, and/or D96T, based on chymotrypsin numbering; modification in the S3 position of MT-SP1 to recognize a leucine in the P3 position of the substrate can include amino acid modifications Q192L, Q192I, Q192F, and/or Y146F, based on chymotrypsin numbering; and/or modifications in the S2 position of MT-SP1 to recognize a leucine in the P2 position of the substrate can include amino acid modifications F99A, F99V, F99S, and/or F99G, based on chymotrypsin numbering. In another example, to modify an MT-SP1 set forth in SEQ ID NO: 2 or 10 to have increased specificity and/or selectivity for a LPSR Factor I cleavage sequence in C3b, modifications in the S4 position of MT-SP1 to recognize a leucine in the P4 position of the substrate can include amino acid modifications W215F, W215Y, Q174F, Q174V, Q174L, Q174Y, and/or M180E, based on chymotrypsin numbering; modifications in the S3 position of MT-SP1 to recognize a proline in the P3 position of the substrate can include amino acid modifications Q192K, Q192R, Q192R, based on chymotrypsin numbering; and/or modifications in the S2 position of MT-SP1 to recognize a serine in the P2 position of the substrate can

include amino acid modifications F99Y, based on chymotrypsin numbering. In an additional example, to modify an MT-SP1 set forth in SEQ ID NO: 2 or 10 to have increased specificity and/or selectivity for a HRGR Factor I cleavage sequence in C4b, modifications in the S4 position of MT-SP1 to recognize a histidine in the P4 position of the substrate can include amino acid modifications W215F, W215Y, Q174A, Q174V, Q174F, Q174R, and/or Q174K, based on chymotrypsin numbering; modifications in the S3 position of MT-SP1 to recognize an arginine in the P3 position of the substrate can include amino acid modifications D217A, D217V, and/or Q192E, based on chymotrypsin numbering; and/or modification is the S2 position of MT-SP1 to recognize a glycine in the P2 position of the substrate can include amino acid modifications F99W, F99Y, and/or F99D, based on chymotrypsin numbering. Exemplary modifications of an MT-SP1 protease scaffold are summarized in Table 15. Combinations of modifications of the noted positions also are contemplated. Any method known in the art to effect mutation of any one or more amino acids in a target protein can be employed. Methods include standard site-directed mutagenesis (using *e.g.*, a kit, such as kit such as QuikChange available from Stratagene) of encoding nucleic acid molecules, or by solid phase polypeptide synthesis methods.

Table 15: Exemplary modifications in MT-SP1 to alter target specificity to Factor I cleavage sequence

	S4				S3			S2
	D96	**Q174**	**M180**	**W215**	**D217**	**Y146**	**Q192**	**F99**
SLLR	A,V, F, S, T	H			Q, N, H	F	L, I, F	A, V, S, G
LPSR		F,V, L,Y	E	F, Y			K, R, Y	Y
HRGR		A, V, F, R, K		F, Y	A, V		E	W, Y

i. Synthesis of Positional Scanning Libraries and Screening using Fluorescence

A protease, modified at any one or more of the S1-S4 subsites can be verified for P1-P4 substrate specificity at any given sub-site using a positional scanning synthetic combinatorial library (PS-SCL) containing a combinatorial fluorogenic substrate library (Harris *et al.*, (2000) *PNAS* 97:7754; US 2004/0175777; US

2004/0146938). A PS-SCL strategy allows for the rapid and facile determination of proteolytic substrate specificity at any one or more S1-S4 active site sub-sites. A PS-SCL strategy involves the use of libraries of peptides whereby one position in the library is held constant, while the remaining positions are composed of all combinations of amino acids used to prepare the library. The use of a combinatorial fluorogenic peptide substrate library, such as for example a 7-amino-4-methylcoumarin (AMC) fluorogenic peptide substrate or a 7-amino-4-carbamoylmethylcoumarin (ACC) fluorogenic peptide substrate, can be used to assay for the activity of a modified protease whereby a fluorogenic moiety is released from a peptide substrate upon action of the protease. Those of skill in the art will appreciate that these methods provide a wide variety of alternative library formats. In one example, a protease can be profiled with a P1-diverse library. A P1-diverse tetrapeptide library contains ACC- or AMC- fluorogenic tetrapeptides whereby the P1 position is systematically held constant while the P2, P3, and P4 positions contain an equimolar mixture of any one or more of the 20 amino acids. An ACC P1-fixed library allows for the verification of the P4, P3, and P2 specificities of any one of the modified proteases. In another example, fixing the P2-position as a large hydrophobic amino acid can circumvent preferential internal cleavage by papain-fold proteases and lead to proper register of the substrate sequence. Determination and consideration of particular limitations relevant to any particular enzyme or method of substrate sequence specificity determination are within the ability of those of skill in the art.

Those of skill in the art will recognize that many methods exist to prepare the peptides. In an exemplary embodiment, the substrate library is screened by attaching a fluorogenically tagged substrate to a solid support. In one example, the fluorogenic leaving group from the substrate peptide is synthesized by condensing an N-Fmoc coumarin derivative, to acid-labile Rink linker to provide ACC resin (Backes *et al.*, (2000) *Nat Biotechnol.* 18:187). Fmoc-removal produces a free amine. Natural, unnatural and modified amino acids can be coupled to the amine, which can be elaborated by the coupling of additional amino acids. In an alternative embodiment, the fluorogenic leaving group can be 7-amino-4-methylcoumarin (AMC) (Harris *et al.*, (2000) *PNAS* 97:7754). After the synthesis of the peptide is complete, the

peptide-fluorogenic moiety conjugate can be cleaved from the solid support, or alternatively, the conjugate can remain tethered to the solid support.

Typically, a method of preparing a fluorogenic peptide or a material including a fluorogenic peptide includes: (a) providing a first conjugate containing a fluorogenic moiety covalently bonded to a solid support; (b) contacting the first conjugate with a first protected amino acid moiety and an activating agent, thereby forming a peptide bond between a carboxyl group and the amine nitrogen of the first conjugate; (c) deprotecting, thereby forming a second conjugate having a reactive amine moiety; (d) contacting the second conjugate with a second protected amino acid and an activating agent, thereby forming a peptide bond between a carboxyl group and the reactive amine moiety; and (e) deprotecting, thereby forming a third conjugate having a reactive amine moiety. In an exemplary embodiment, the method further includes: (f) contacting the third conjugate with a third protected amino acid and an activating agent, thereby forming a peptide bond between a carboxyl group and the reactive amine moiety; and (e) deprotecting, thereby forming a fourth conjugate having a reactive amine moiety.

For amino acids that are difficult to couple (*e.g.*, Ile, Val, *etc.*), free, unreacted amine can remain on the support and complicate subsequent synthesis and assay operations. A specialized capping step employing the 3-nitrotriazole active ester of acetic acid in DMF efficiently acylates the remaining aniline. The resulting acetic-acid capped coumarin that can be present in unpurified substrate sequence solution is generally not a protease substrate sequence.

Solid phase peptide synthesis in which the C-terminal amino acid of the sequence is attached to an insoluble support followed by sequential addition of the remaining amino acids in the sequence is an exemplary method for preparing the peptide backbone of the polypeptides provided herein. Techniques for solid phase synthesis are described by Narany and Merrifield, Solid-Phase Peptide Synthesis; pp.3-284 in The *Peptides: Analysis, Synthesis, Biology*. Vol. 2; *Special Methods in Peptide Synthesis*, Part A., Gross and Meienhofer, eds. Academic press, N.Y., (1980); and Stewart et al., (1984) *Solid Phase Peptide Synthesis*, 2nd etd. Pierce Chem. Co.,

Rockford, Ill. Solid phase synthesis is most easily accomplished with commercially available peptide synthesizers utilizing Fmoc or t-BOC chemistry.

For example, peptide synthesis can be performed using well known Fmoc synthesis chemistry. For example, the side chains of Asp, Ser, Thr, and Tyr are protected using t-butyl and the side chain of Cys residue using S-trityl and S-t-butylthio, and Lys residues are protected using t-Boc, Fmoc and 4-methyltrityl. Appropriately protected amino acid reagents are commercially available or can be prepared using art-recognized methods. The use of multiple protecting groups allows selective deblocking and coupling of a fluorophore to any particular desired side chain. Thus, for example, t-Boc deprotection is accomplished using TFA in dichloromethane. Fmoc deprotection is accomplished using, for example, 20% (v/v) piperidine in DMF or N-methylpyrolidone, and 4-methyltrityl deprotection is accomplished using, for example, 1 to 5% (v/v) TFA in water or 1% TFA and 5% triisopropylsilane in DCM. A-t-butylthio deprotection is accomplished using, for example, aqueous mercaptoethanol (10%). Removal of t-buyl, t-boc, and S-trityl groups is accomplished using, for example TFA:phenol:water:thioaniso:ethanedithio (85:5:5:2.5:2.5), or TFA:phenol:water (95:5:5).

Diversity at any particular position or combination of positions can be introduced using a mixture of at least two, six, 12, 20 or more amino acids to grow the peptide chain. The mixtures of amino acids can include any useful amount of a particular amino acid in combination with any useful amount of one or more different amino acids. In one embodiment, the mixture is an isokinetic mixture of amino acids (a mixture in appropriate ratios to allow for equal molar reactivity of all components).

Modified proteases can be combined to acquire the specificity of multiple modified proteases. A mutation at one residue of a scaffold, which produces specificity at one site, is combined in the same protease with another mutation at another site on the scaffold to make a combined specificity protease. Any number of mutations at discrete sites on the same scaffold can be used to create a combined specificity protease.

Modified proteases, such as for example a modified MT-SP1 protease, that match the desired specificity profile, can then be assayed using individual fluorogenic

peptide substrates corresponding to the desired cleavage sequence. A method of assaying for a modified protease that can cleave any one or more of the Factor I cleavage sequences includes: (a) contacting a peptide fluorogenic sample (containing a Factor I cleavage sequence) with a protease, in such a manner whereby a fluorogenic moiety is released from a peptide substrate sequence upon action of the protease, thereby producing a fluorescent moiety; and (b) observing whether the sample undergoes a detectable change in fluorescence, the detectable change being an indication of the presence of the enzymatically active protease in the sample. In such an example an ACC- or AMC- tetrapeptide such as Ac-SLLR-AMC or Ac-HRGR-AMC can be made and incubated with a modified protease and activity of the protease can be assessed by assaying for release of the fluorogenic moiety.

Assaying for a protease in a solution simply requires adding a quantity of the stock solution of a protease to a fluorogenic protease indicator peptide and measuring the subsequent increase in fluorescence or decrease in excitation band in the absorption spectrum. The solution and the fluorogenic indicator also can be combined and assayed in a "digestion buffer" that optimizes activity of the protease. Buffers suitable for assaying protease activity are well known to those of skill in the art. In general, a buffer is selected with a Ph which corresponds to the Ph optimum of the particular protease. For example, a buffer particularly suitable for assaying elastase activity contains 50mM sodium phosphate, 1 mM EDTA at pH 8.9. The measurement is most easily made in a fluorometer, an instrument that provides an "excitation" light source for the fluorophore and then measures the light subsequently emitted at a particular wavelength. Comparison with a control indicator solution lacking the protease provides a measure of the protease activity. The activity level can be precisely quantified by generating a standard curve for the protease/indicator combination in which the rate of change in fluorescence produced by protease solutions of known activity is determined.

While detection of fluorogenic compounds can be accomplished using a fluorometer, detection also can be accomplished by a variety of other methods well known to those of skill in the art. Thus, for example, when the fluorophores emit in the visible wavelengths, detection can be simply by visual inspection of fluorescence

in response to excitation by a light source. Detection also can be by means of an image analysis system utilizing a video camera interfaced to a digitizer or other image acquisition system. Detection also can be by visualization through a filter, as under a fluorescence microscope. The microscope can provide a signal that is simply visualized by the operator. Alternatively, the signal can be recorded on photographic film or using a video analysis system. The signal also can simply be quantified in real time using either an image analysis system or a photometer.

Thus, for example, a basic assay for protease activity of a sample involves suspending or dissolving the sample in a buffer (at the pH optima of the particular protease being assayed), adding to the buffer a fluorogenic protease peptide indicator, and monitoring the resulting change in fluorescence using a spectrofluorometer as shown in *e.g.*, Harris *et al.*, (1998) *J Biol Chem* 273:27364. The spectrofluorometer is set to excite the fluorophore at the excitation wavelength of the fluorophore. The fluorogenic protease indicator is a substrate sequence of a protease that changes in fluorescence due to a protease cleaving the indicator.

Modified proteases also are assayed to ascertain that they will cleave the desired sequence when presented in the context of the full-length protein. The target substrate proteins containing Factor I cleavage sites are in the C3 and C4 sequences, specifically in C3b and C4b which are generated from C3 and C4, respectively, following convertase activation. Factor I also cleaves iC3 and iC4 which are altered species forms of C3 and C4. Methods to assess cleavage of a target protein are described herein and/or are well known in the art. In one example, a purified complement protein, C3b, C4b, iC3, or iC4, can be incubated in the presence or absence of a modified protease and the cleavage event can be monitored by SDS-PAGE followed by Coomassie Brilliant Blue staining for protein and analysis of cleavage products using densitometry. The activity of the target protein also is assayed, such as, for example in a hemolysis assay, using methods described herein or that are well known in the art, to verify that its function has been destroyed by the cleavage event.

b. Empirical Modification

A library of modified proteases can be generated by mutating any one or more amino acid residues of a protease using any method commonly known in the art (see also published U.S. Appln. No. 2004/0146938). The library of modified proteases can be tested in functional assays of complement activation to determine if they are "Hits" for inhibiting complement activation. The target complement substrate of the modified protease can be identified, and the peptide cleavage sequence can be determined.

In one example, any one or more amino acids of a protease are mutated using any standard site-directed mutagenesis kit such as for example QuikChange (Stratagene). In another example, any one or more amino acids of a protease are mutated by saturation mutagenesis of active site residues. In this example, residues that form the S1-S4 pocket of a protease (where the protease is in contact with the P1-P4 residues of the peptide substrate) and/or that have been shown to be important determinants of specificity are mutated to every possible amino acid, either alone or in combination. In some cases, there is little (if any) interaction between the S1-S4 pockets of the active site, such that each pocket appears to recognize and bind the corresponding residue on the peptide substrate sequence independent of the other pockets. Thus, the specificity determinants generally can be changed in one pocket without affecting the specificity of the other pockets. In one exemplary embodiment, a saturation mutagenesis technique is used in which the residue(s) lining the pocket are mutated to each of the 20 possible amino acids (see for example the Kunkle method, Current Protocols in Molecular Biology, John Wiley and Sons, Inc., Media Pa.). In such a technique, a mutagenic oligonucleotide primer is synthesized which contains either NNS or NNK-randomization at the desired codon. The primer is annealed to the single stranded DNA template and DNA polymerase is added to synthesize the complementary strand of the template. After ligation, the double stranded DNA template is transformed into *E.coli* for amplification.

Amino acids that form the extended substrate binding pocket of exemplary proteases are described herein. Generally, the substrate specificity of a protease is known such as for example by molecular modeling based on three-dimensional structures of the complex of a protease and substrate (see for example, Wang *et al.*,

(2001) *Biochemistry* 40(34):10038; Hopfner *et al., Structure Fold Des.* 1999 7(8):989; Friedrich *et al.*, (2002) *J Biol Chem* 277(3):2160; Waugh *et al.*, (2000) *Nat Struct Biol.* 7(9):762). In one example, mutations of MT-SP1 can be in any one or more residues (based on chymotrypsin numbering) that contribute to substrate specificity including 195, 102, 57 (the catalytic triad); 189, 190, 191, 192, 216 and 226 (S1); 57, 58, 59, 60, 61, 62, 63, 64, 99 (S2); 146, 192, 217, 218 (S3); 96, 97, 98, 99, 100, 168, 169, 170, 170A, 171, 172, 173, 174, 175, 176, 178, 179, 180, 215, 217, 224 (S4). In another example, mutation of amino acid residues in a papain family protease can be in any one or more residues that affect P2 specificity (standard papain numbering) including 66-68, 133, 157, 160, and/or 215. In addition, residues that do not directly contact the protease substrate, but do affect the position and/or conformation of contact residues (such as for example those listed above) also can be mutated to alter the specificity of a protease scaffold.

To identify those modified proteases that target any one or more of the complement proteins, a library of modified proteases generated from a protease scaffold, such as for example an MT-SP1 scaffold, are tested in functional assays of complement activation. Assays for complement activation are described herein and can include any one or more of hemolytic assays and/or assays to detect activation products of one or more of the complement cascades. For example, enzyme immunoassays or ELISAs can be used to detect the presence of cleavage products of complement activation such as for example C4a, C5a, C3b, C3d, and C5-b9. Modified proteases that inhibit the activation of complement (such as by increasing CH50 levels as determined by a hemolytic assay or decreasing the detection of a complement cleavage product) can be identified as a "Hit". In one embodiment, combinations of "Hits" can be made to further increase the specificity and/or selectivity of a protease for inhibiting complement activation.

Modified proteases, such as for example a modified MT-SP1, that are identified as "Hits" for inhibiting complement activation in functional assays can be screened to determine the complement protein target substrate. Assays to detect for cleavage of a complement protein are described herein. In one example, a purified complement protein can be incubated in the presence or absence of a modified

protease and analyzed and resolved on an SDS-PAGE gel and the protein cleavage products can be detected following staining with a protein stain such as Coomassie Brilliant Blue. Cleavage products can be excised and the peptide cleavage sequence can be determined by N-terminal sequencing. Using the identified peptide cleavage sequence as determined by empirically testing a library of modified proteases, further modified proteases can be identified and generated using the rational approach described above for Factor I cleavage sequences.

2. Methods of assessing specificity

Provided herein are methods of assessing substrate specificity of the resulting scaffold or modified proteases. In one embodiment, the specificity of any one or more of the S1-S4 sub-sites can be determined using ACC or AMC positional scanning libraries as discussed above. In another embodiment the specificity of a scaffold or modified protease for a target substrate compared to a non-target substrate can be determined using single substrate kinetic assays, see *e.g.*, Harris, *et al.* (2000) *PNAS*, 97:7754. In specific embodiments, comparison of the specificities of a target protease and a scaffold protease can be used to determine if the modified protease exhibits altered, for example, increased, specificity compared to a scaffold protease.

The specificity of a protease for a target substrate can be measured by observing how many disparate sequences a modified protease cleaves at a given activity compared to a scaffold protease. If the modified protease cleaves fewer target substrates than the wildtype protease, the modified protease has greater specificity than the scaffold protease for those target substrates. The specificity of a protease for a target substrate can be determined from the specificity constant of cleavage of a target substrate compared to a non-target substrate (*i.e.* a native wildtype substrate sequence of a protease). A ratio of the specificity constants of a modified protease for a target substrate versus a non-target substrate can be made to determine a ratio of the efficiency of cleavage of the protease. Comparison of the ratio of the efficiency of cleavage between a modified protease and a scaffold protease can be used to assess the fold change in specificity for a target substrate. The fold change is an increase in specificity of a modified protease for a target substrate compared to a scaffold protease that is sufficient to achieve a predetermined alteration in complement

activation or in a complement-mediated activity. Specificity can be at least 2-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200,300, 400, 500, 600, 700, 800, 900, 1000-fold or more when compared to the specificity of a scaffold protein for a target substrate versus a non-target substrate.

In one example, a modified protease that matches the desired specificity profiles, as determined by using positional scanning substrate libraries, can be assayed using individual peptide substrates corresponding to the desired target cleavage sequence compared to a non-target substrate cleavage sequence to determine the magnitude and change in specificity. In one embodiment, the individual peptide cleavage sequences can be attached to a fluorogenically tagged substrate, such as for example an ACC or AMC fluorogenic leaving group such as is described herein, and the release of the fluorogenic moiety can be determined as a measure of specificity of a protease for a peptide cleavage sequence. The rate of increase in fluorescence of a non-target substrate cleavage sequence or target cleavage sequence can be measured such as by using a fluorescence spectrophotometer. The rate of increase in fluorescence can be measured over time. Michaelis-Menton kinetic constants can be determined by the standard kinetic methods. The kinetic constants k_{cat}, K_m and k_{cat}/K_m can be calculated by graphing the inverse of the substrate concentration versus the inverse of the velocity of substrate cleavage, and fitting to the Lineweaver-Burk equation ($1/velocity=(K_m/V_{max})(1/[S]) + 1/V_{max}$; where $V_{max}=[ET]k_{cat}$). The specificity constant (k_{cat}/K_m) is a measure of how well a substrate is cut by a particular protease.

In one embodiment, a non-target substrate cleavage sequence can be a native substrate cleavage sequence, such as a cleavage sequence recognized by wildtype MT-SP1. For example, efficient auto-activation of MT-SP1 entails recognition and cleavage of an Arg-Gln-Ala-Arg P4-P1 target sequence. MT-SP1 also can efficiently activate the proteinase-activated receptor-2 (PAR2), single chain uPA, and the hepatocyte growth factor/scatter factor. These extracellular surface-localized proteins display the P4 to P1 target sequences Ser-Lys-Gly-Arg, Pro-Arg-Phe-Lys, and Lys-Gln-Gly-Arg, respectively, which match closely the MT-SP1 cleavage specificity

requirements observed for small peptidic substrates. In one embodiment, a fluorogenically tagged tetrapeptide of RQAR (SEQ ID NO: 401), or SLGR (SEQ ID NO: 392), or PRFK (SEQ ID NO: 402), or KQGR (SEQ ID NO: 403) can be used as a non-target substrate cleavage sequence.

In another embodiment, any one or more of the cleavage sequences of a complement protein can be determined and used as a desired target cleavage sequence. For example, any one or more of the Factor I cleavage sequences, such as for example SLLR (SEQ ID NO: 389), LPSR (SEQ ID NO: 388), and HRGR (SEQ ID NO: 390) can be used as a fluorogenically tagged tetrapeptide target cleavage sequence. In another example, the desired cleavage sequence in a complement protein targeted by any one or more wildtype or modified protease can be empirically determined by N-terminally sequencing cleavage products upon cleavage of any one or more of the complement proteins by a protease. In such an example, any one or more of the cleavage sequences identified as target cleavage sequences of a protease provided herein can be used, including those described in Example 3. Therefore, for example, a fluorogenically tagged tetrapeptide of GATR (SEQ ID NO: 391), SLGR (SEQ ID NO: 392), VFAK (SEQ ID NO: 393), REFK (SEQ ID NO: 394), QHAR (SEQ ID NO: 398), GLAR (SEQ ID NO: 395), RLGR (SEQ ID NO: 396), AEGK (SEQ ID NO: 397), or HRGR (SEQ ID NO: 390) can be used as a target substrate cleavage sequence.

In an additional embodiment, a full length complement protein can be used as a target substrate to assay for protease specificity compared to a full length native target substrate of a protease. Further, a full length complement protein can be used to assess the correlation between substrate specificity and cleavage by a protease of a full length target substrate versus a four amino acid P1-P4 substrate cleavage sequence contained within the target substrate. In one example, a full length C2 protein can be used as a desired cleavage target of any one or more or the proteases to assess specificity. In this example, cleavage of C2 by a modified or scaffold protease can be compared to cleavage of another full-length substrate, or the cleavage can be compared to a fluorogenic tetrapeptide cleavage sequence of C2, such as those described in Example 11 (i.e., GATR, SLGR, or VFAK). The specificity constant of

cleavage of a full length protein by a protease can be determined by using gel densitometry to assess changes in densitometry over time of a full-length target substrate band incubated in the presence of a protease.

3. Protease polypeptides

Using the methods described herein, proteases are provided that cleave any one or more of the complement proteins, whereby cleavage of the complement protein inhibits complement activation. As provided herein, a protease polypeptide that cleaves any one or more of the complement proteins is a non-complement protease. A protease polypeptide can include the amino acid sequence of a scaffold protease whose sequence is provided herein, such as in any one of SEQ ID NOS: 2, 4, 8, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 269, 270, 272, 274, 276, 278, 280, 282, 284, 286, 287, 289, 291, 293, 295, 297, 373, 375, 377, 379, 381, 383, 385, 387, 544, 545, 547, 549, and 551, or a catalytically active portion thereof. For example, the scaffold protease can be a wildtype or prominent form of the protease. In another embodiment, the scaffold protease can be an allelic variant of a protease. The scaffold protease is of mammalian origin, particularly human origin, although the scaffold protease polypeptide sequence also can be from any one or more of hamster, mouse, rat, cow, monkey, orangutan, baboon, chimpanzee, macaque, gibbon or gorilla origin. In other embodiments, the scaffold protease can be from non-mammalian origin such as from a plant or parasite.

In one embodiment, a protease scaffold is modified to have increased specificity and/or selectivity to any one or more complement proteins compared to the scaffold protease, while still encoding a protein that maintains its protease activity. Modified protease polypeptides include those with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more modified positions. Generally, a modified protease includes any variant in which residues at a particular position in the sequence

have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the wildtype protease protein as well as the possibility of deleting one or more residues form the wildtype protease sequence. Any amino acid substitution, insertion, or deletion of a wildtype protease sequence is provided herein.

Provided herein are modified polypeptides that contain a full length sequence of a scaffold protease, but that contain modifications in any one or more amino acids that contribute to substrate specificity and/or selectivity. In one embodiment, the modified protease polypeptides provided herein have increased substrate specificity and/or selectivity for any one or more complement protein compared to a scaffold protease, whereby cleavage of a complement protein inhibits complement activation. In another embodiment, a modified protease polypeptide has a greater specificity for cleavage of a complement protein compared to a VEGF or VEGFR. In an additional embodiment, the modified proteases provided herein do not cleave a VEGF or VEGFR. Further, a modified protease polypeptide provided herein containing modifications in any one or more amino acids that contribute to substrate specificity and/or selectivity, also can contain other modifications in regions that are non-essential to the substrate specificity of a protease.

Modified protease polypeptides provided herein also can contain a catalytically active portion of a full-length scaffold or unmodified protease. When the polypeptide includes a catalytically active portion it can include other non-protease portions in addition thereto as long as the resulting polypeptide exhibits protease activity at least 1%, 2%, 5%, 10%, 20%, 50%, 100% or more of the full-length polypeptide. In addition the catalytically active portion is less than the full-length by at least one amino acid, and can be less than the full-length protease domain as long as protease activity is retained. A catalytically active portion of a protease containing modifications in any one or more amino acids that contribute to substrate specificity can be an active single-chain or double-chain form of a scaffold protease. In some embodiments, a modified protease can be substituted into another polypeptide, either at the N- or C- terminus, such as in a fusion protein. In additional embodiments, a modified polypeptide protease, such as for example a catalytically active portion

thereof of a modified protease, can be inserted to replace the protease domain from another protease.

Provided herein are proteases exhibiting increased specificity and/or selectivity to any one or more complement proteins having a sequence of amino acids encompassed in any one of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, 344, 660-662 or a fragment thereof that exhibits complement activity.

a. MT-SP1 polypeptides

Provided herein are MT-SP1 polypeptides that cleave any one or more of the complement proteins, whereby cleavage of the complement protein inhibits complement activation. An MT-SP1 polypeptide provided herein can be a full-length MT-SP1 polypeptide (SEQ ID NO:2) or can be a fragment or partial sequence of full-length MT-SP1 that exhibits catalytic activity. In one example, an MT-SP1 polypeptide can be a single-chain protease domain of MT-SP1 (SEQ ID NO: 10). In another embodiment, an MT-SP1 polypeptide can be any one or more of the allelic variants of MT-SP1 as set forth in SEQ ID NO:448.

Also provided herein are modified MT-SP1 polypeptides containing modifications in any one or more amino acids of a scaffold MT-SP1 polypeptide using any one of the methods described herein. In one embodiment, the modifications can be made in a scaffold MT-SP1 set forth in SEQ ID NO:2, or can be made in any allelic variant of a wildtype MT-SP1 such as for example any one of the allelic variants set forth in SEQ ID NO:448. A modified MT-SP1 polypeptide provided herein can constitute a full-length sequence of an MT-SP1 scaffold, or can constitute a catalytically active portion thereof of a full-length MT-SP1 scaffold protease. The modified MT-SP1 exhibits an increase in the specificity and/or selectivity to any one or more of the complement proteins compared to a MT-SP1 scaffold, whereby cleavage of the protein inhibits complement activation.

Provided herein are modified MT-SP1 polypeptides with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more modified positions. In one embodiment, a modified MT-SP1 polypeptide includes mutation of any one or more amino acids in the extended substrate binding pocket of MT-SP1 including, for

example, modification of any one or more amino acid residues of 195, 102, 57 (the catalytic triad); 189, 190, 191, 192, 216 and 226 (S1); 57, 58, 59, 60, 61, 62, 63, 64, 99 (S2); 146, 192, 217, 218 (S3); 96, 97, 98, 99, 100, 168, 169, 170, 170A, 171, 172, 173, 174, 175, 176, 178, 179, 180, 215, 217, 224 (S4), based on chymotrypsin numbering. Modifications in the protease domain of MT-SP1 to alter substrate specificity and/or selectivity also include modification of any one or more amino acid residues of 41, 60c, 143, 147, 151or 221a, based on chymotrypsin numbering.

Provided herein are modified MT-SP1 polypeptides where the following amino acid residues were identified in the protease domain of MT-SP1 as increasing the specificity and/or selectivity of cleavage of any one or more complement protein thereby inhibiting complement activation: 41, 60c, 97, 143, 146, 147, 151, 172, 175, 192, 217, 221a, and 224 based on chymotrypsin numbering. The modified MT-SP1 polypeptides exhibit increased specificity and/or selectivity towards any one or more of the complement components compared to a wildtype MT-SP1 of SEQ ID NO: 2 or a catalytically active portion thereof set forth in SEQ ID NO:10. Thus, provided herein are modified MT-SP1 polypeptides exhibiting increased specificity and/or selectivity towards any one or more complement components containing a modification at an amino acid position corresponding to any one or more amino acid residues selected from among I41, $R60_C$, F97, H143, Y146, G147, G151, L172, Q175, Q192, D217, $Q221_a$ or K224 in an MT-SP1 set forth in SEQ ID NO: 2 or SEQ ID NO:10, based on chymotrypsin numbering. In one embodiment, amino acid replacement or replacements correspond to any of the following positions: I41T, I41A, I41L, I41F, I41D, I41E, $R60_CD$, $R60_CW$, F97D, F97E, F97A, F97W, H143V, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Y146F, G147E, G151L, L172N, Q175D, Q175E, Q175H, Q175L, Q175F, Q175W, Q175Y, Q175R, Q175K, Q192A, Q192R, Q192V, Q192F, D217F, $Q221_aD$, $Q221_aL$, $Q221_aE$, K224A, K224L, K224R, K224N, K224T, K224Y, K224S and K224F of the protease domain of MT-SP1 based on chymotrypsin numbering. Table 16 provides non-limiting examples of amino acid replacements that increase specificity and/or selectivity to any one or more complement protein, including SEQ ID NOS for exemplary polypeptide sequences and the encoding nucleic acid sequences.

Table 16:

ID #	Modification	Full-length SEQ ID NOS: (aa, nt)	Catalytically active portion SEQ ID NOS: (aa, nt)
CB200	wildtype	1, 2	10, 9
CB12	F97D	406, 482	16, 15
CB13	F97E	407, 483	18, 17
CB16	Y146F	646	592
CB17	L172N	647	593
CB20	Q175D	636	582
CB21	Q175E	635	581
CB31	F97A	408, 484	20, 19
CB32	F97W	409, 485	22, 21
CB40	Y146N	410, 486	24, 23
CB41	Y146D	411, 487	26, 25
CB42	Y146E	412, 488	28, 27
CB43	Y146A	413, 489	30, 29
CB44	Y146W	414, 490	32, 31
CB45	Y146R	415, 491	34, 33
CB62	Q192V	405, 481	14, 13
CB64	Q192R	416, 492	36, 35
CB66	K224A	417, 493	38, 37
CB67	K224F	418, 494	40, 39
CB80	$R60_cD$	623	569
CB82	$R60_cW$	621	567
CB268	Q221aD	614	560
CB274	G147E	622	568

Also provided herein are modified MT-SP1 polypeptides where the following amino acid residues were identified in the substrate binding site S1-S4 of MT-SP1 as increasing the specificity and/or selectivity of cleavage of any one or more complement protein containing a SLLR/SE Factor I cleavage sequence, thereby inhibiting complement activation: 96, 174, 217, 146, 192, and 99, based on chymotrypsin numbering. The modified MT-SP1 polypeptides exhibit increased specificity and/or selectivity towards a C3b or iC3 complement protein substrate compared to a native target substrate of wildtype MT-SP1 of SEQ ID NO: 2 or a catalytically active portion thereof set forth as SEQ ID NO:10. In one embodiment, amino acid replacement or replacements correspond to any of the following positions: D96A, D96V, D96F, D96S, D96T, Q174H, D217Q, D217N, D217H, Q192L, Q192I,

Q192F, F99A, F99V, F99S, or F99G of the protease domain of MT-SP1 based on chymotrypsin numbering. Table 17 provides non-limiting examples of amino acid replacements that increase specificity and/or selectivity to any one or more complement protein, including SEQ ID NOS for exemplary polypeptide sequences and the encoding nucleic acid sequences.

Table 17:

Modification	Full-length SEQ ID NOS:	Catalytically active portion SEQ ID NOS:
D96A	423, 499	45, 455
D96V	424, 500	46, 456
D96F	425, 501	47, 457
D96S	426, 502	48, 458
D96T	427, 503	49, 459
Q174H	419, 495	41, 451
D217Q	420, 496	42, 452
D217N	421, 497	43, 453
D217H	422, 498	44, 454
Q192L	428, 504	50, 460
Q192I	429, 505	51, 461
Q192F	430, 506	52, 462
Y146F	431, 507	53, 463
F99A	432, 508	54, 464
F99V	433, 509	55, 465
F99S	434, 510	56, 466
F99G	435, 511	57, 467

Also provided herein are modified MT-SP1 polypeptides where the following amino acid residues were identified in the substrate binding site S1-S4 of MT-SP1 as increasing the specificity and/or selectivity of cleavage of any one or more complement protein containing a LPSR/KI Factor I cleavage sequence, thereby inhibiting complement activation: 174, 180, 215, 192, and 99, based on chymotrypsin numbering. The modified MT-SP1 polypeptides exhibit increased specificity and/or selectivity towards a C3b or iC3 complement protein substrate compared to a native target substrate of wildtype MT-SP1 of SEQ ID NO: 2 or a catalytically active portion thereof set forth as SEQ ID NO:10. In one embodiment, amino acid replacement or replacements correspond to any of the following positions: Q174F, Q174V, Q174L, Q174Y, M180E, W215F, W215Y, Q192K, Q192R, Q192Y, or F99Y of the protease domain of MT-SP1 based on chymotrypsin numbering. Table 18 provides non-limiting examples of amino acid replacements that increase specificity and/or

selectivity to any one or more complement protein, including SEQ ID NOS for exemplary polypeptide sequences and the encoding nucleic acid sequences.

Table 18:

Modification	Full-length SEQ ID NOS:	Catalytically active portion SEQ ID NOS:
Q174F	440, 516	62, 472
Q174V	439, 515	61, 471
Q174L	529, 539	524, 534
Q174Y	530, 540	525, 535
M180E	531, 541	526, 536
W215F	436, 512	58, 468
W215Y	437, 513	59, 469
Q192K	532, 542	527, 537
Q192R	416, 492	35, 36
Q192Y	533, 543	528, 538
F99Y	447, 523	69, 479

Also provided herein are modified MT-SP1 polypeptides where the following amino acid residues were identified in the substrate binding site S1-S4 of MT-SP1 as increasing the specificity and/or selectivity of cleavage of any one or more complement protein containing a HRGR/TL Factor I cleavage sequence, thereby inhibiting complement activation: 174, 215, 192, 217, and 99 based on chymotrypsin numbering. The modified MT-SP1 polypeptides exhibit increased specificity and/or selectivity towards a C4b or iC4 complement protein substrate compared to a native target substrate of wildtype MT-SP1 of SEQ ID NO: 2 or a catalytically active portion thereof set forth as SEQ ID NO:10. In one embodiment, amino acid replacement or replacements correspond to any of the following positions: W215F, W215Y, Q174A, Q174V, Q174F, Q174R, Q174K, D217A, D217V, Q192E, F99W, and F99Y of the protease domain of MT-SP1 based on chymotrypsin numbering. Table 19 provides non-limiting examples of amino acid replacements that increase specificity and/or selectivity to any one or more complement protein, including SEQ ID NOS for exemplary polypeptide sequences and the encoding nucleic acid sequences.

Table 19:

Modification	Full-length SEQ ID NOS:	Catalytically active portion SEQ ID NOS:
W215F	436, 512	58, 468

W215Y	437, 513	59, 469
Q174A	438, 514	60, 470
Q174V	439, 515	61, 471
Q174F	440, 516	62, 472
Q174R	441, 517	63, 473
Q174K	442, 518	64, 474
D217A	443, 519	65, 475
D217V	444, 520	66, 476
Q192E	445, 521	67, 477
F99W	446, 522	68, 478
F99Y	447, 523	69, 479

In one embodiment, modified proteases can be combined such as, for example, to acquire the specificity of multiple proteases. A mutation at one residue of a protease scaffold, which produces specificity at one site of a substrate sequence, can be combined in the same protease with another mutation at another site of the protease scaffold sequence to make a combined specificity protease. Any number of mutations at discrete sites on the same protease scaffold an be used to create a combined specificity protease. A modified protease can contain 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more mutations by combining any two or more mutations identified as contributing to substrate specificity and/or selectivity of the protease.

For example, a modified MT-SP1 protease can contain any two or more mutations, such as any two or more mutations set forth above, to generate a combined protease. Provided herein are modified MT-SP1 polypeptides having two or more modifications corresponding to any of positions 41, 60c, 96, 97, 99, 143, 146, 147, 151, 172, 174, 175, 192, 215, 217, 221a, and 224, based on chymotrypsin numbering. The modified MT-SP1 polypeptide exhibits increased specificity and/or selectivity to any one or more complement components compared to a scaffold or wildtype MT-SP1 of SEQ ID NO: 2 or a catalytically active portion thereof set forth in SEQ ID NO: 10. Thus, provided herein are modified MT-SP1 polypeptides exhibiting increased specificity and/or selectivity towards any one or more complement components containing two or more modifications at an amino acid position corresponding to any two or more amino acid residues selected from among I41, $R60_C$, D96, F97, F99, H143, Y146, G147, G151, L172, Q174, Q175, Q192, W215, D217, $Q221_a$ or K224 in an MT-SP1 set forth in SEQ ID NO: 2 or SEQ ID NO:10,

based on chymotrypsin numbering. In some examples, a modified MT-SP1 containing two or more modifications contains a modification at one or both of position Y146 and K224. In another example, a modified MT-SP1 containing two or more modifications contains a modification at position G151. Modified MT-SP1 polypeptides can be generated using any of the methods disclosed herein. Table 20 provides non-limiting examples of amino acid replacements that increase specificity and/or selectivity to any one or more complement protein, including SEQ ID NOS for exemplary polypeptide sequences and the encoding nucleic acid sequences.

Table 20:

ID #	Modification	Full-length SEQ ID NOS:	Catalytically active portion SEQ ID NOS:
CB155	Y146D/K224F	404, 480	11, 12
CB212	Y146N/K224F	655	601
CB213	Y146E/K224F	642	588
CB214	Y146A/K224F	643	589
CB216	Q192V/K224F	659	605
CB218	Q192F/K224F	657	603
CB219	Y146D/Q192A/K224F	658	604
CB232	Y146E/K224L	620	566
CB235	Y146E/K224A	630	576
CB238	Y146D/K224L	628	574
CB244	Y146D/K224R	617	563
CB245	Y146D/K224N	637	583
CB251	Y146E/K224R	615	561
CB252	Y146E/K224N	606	552
CB255	Y146E/K224T	644	590
CB257	Y146E/K224Y	633	579
CB331	I41D/Y146D/K224L	653	599
CB332	I41E/Y146D/K224L	639	585
CB349	I41D/Y146D/K224F	654	600
CB350	I41E/Y146D/K224F	652	598
CB351	I41T/Y146D/K224F	608	554
CB353	H143V/Y146D/K224F	641	587
CB357	I41T/Y146D/K224L	626	572
CB367	Y146D/Q175D/K224R	624	570
CB373	Y146E/Q175D/K224R	619	565
CB377	Y146E/Q175D/K224N	616	562
CB381	Y146D/Q175H/K224L	631	577
CB383	Y146D/Q175L/K224L	625	571
CB385	Y146D/Q175F/K224L	634	580
CB387	Y146D/Q175W/K224L	627	573

CB388	Y146D/Q175Y/K224L	632	578
CB403	Y146D/D217F/K224L	640	586
CB409	I41A/Y146D/K224F	651	597
CB412	I41L/Y146D/K224F	649	595
CB413	I41F/Y146D/K224F	648	594
CB421	I41T/Y146D/Q175D/K224F	656	602
CB422	I41T/Y146E/Q175D/K224N	609	555
CB423	I41T/Y146E/K224L	645	591
CB450	I41T/I46D/G151L/K224F	650	596
CB451	Y146D/Q221aL/K224S	638	584
CB458	Y146E/Q221aE/K224R	629	575
CB464	Y146E/Q221aE/k224F	611	557
CB476	I41T/Y146D/Q175D/K224L	663	672
CB477	I41T/Y146D/Q175D/K224R	664	673
CB478	I41T/Y146D/Q175D/K224N	665	674
CB480	I41T/Y146D/G151L/Q175D/K224F	666	675
CB481	I41T/Y146D/G151L/Q175D/K224L	667	676
CB482	I41T/Y146D/G151L/Q175D/K224R	668	677
CB483	I41T/Y146D/G151L/Q175D/K224N	669	678
CB484	I41T/Y146E/Q175D/K224F	670	679
CB485	I41T/Y146E/Q175D/K224L	671	680
CB486	I41T/Y146E/Q175D/K224R	607	553
CB487	I41T/Y146E/G151L/Q175D/K224N	613	559
CB488	I41T/Y146E/G151L/Q175D/K224F	618	564
CB489	I41T/Y146E/G151L/Q175D/K224L	610	556
CB490	I41T/Y146E/G151L/Q175D/K224R	612	558
	I41T/Y146D/G151L/K224N	681	696
	Y146D/Q175D/K224N	682	697
	I41T/Y146D/K224N	683	698
	Y146D/G151L/K224N	684	699
	Y146D/Q175R/K224N	685	700
	Y146D/Q175K/K224N	686	701
	Y146D/Q175H/K224N	687	702
	I41T/Y146D/G151L/Q175K/K224F	688	703
	I41T/Y146D/G151L/Q175R/K224F	689	704
	I41T/Y146D/G151L/Q175H/K224F	690	705
	I41T/Y146D/G151L/Q175Y/K224F	691	706
	I41T/Y146D/G151L/Q175K/K224N	692	707
	I41T/Y146D/G151L/Q175R/K224N	693	708
	I41T/Y146D/G151L/Q175H/K224N	694	709
	I41T/Y146D/G151L/Q175Y/K224N	695	710

Provided herein are modified MT-SP1 polypeptides where the replacement(s) are made in an MT-SP1 polypeptide scaffold having a sequence of amino acids set forth in SEQ ID NO:2, where the modified MT-SP1 polypeptide exhibits increased specificity and/or selectivity to any one or more complement components compared

to the unmodified protein. Also provided herein are modified MT-SP1 polypeptides containing replacement(s) in an MT-SP1 scaffold having a sequence of amino acids set forth in SEQ ID NO:10, where the modified MT-SP1 polypeptide exhibits increased specificity and/or selectivity to any one or more complement components compared to the unmodified protein. Such an MT-SP1 scaffold polypeptide is a catalytically active portions thereof of an MT-SP1 polypeptide. Exemplary modified MT-SP1 polypeptides provided herein containing modification(s) of a catalytically active portion thereof of a full-length MT-SP scaffold have a sequence of amino acids as set forth in any one of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 524-528, 552-605, 672-680, or 696-710. Exemplary modified MT-SP1 polypeptides provided herein containing modification(s) of a full-length MT-SP1 scaffold have a sequence of amino acids as set forth in any one of SEQ ID NOS: 404-418-447, 529-533, 606-659, 663-671, or 681-695.

E. Assays to assess or monitor modified protease activities on complement-mediated functions

A modified protease can exhibit alterations in specificity and/or selectivity to any one or more complement proteins and thereby inactivate any one or more complement proteins compared to the corresponding full-length, scaffold or wildtype form of the complement protein. Modified proteases retain their protease activity, but can exhibit an increased specificity and/or selectivity to any one or more complement proteins. Exemplary proteases specifically cleave any one or more complement protein and thereby alter the activity of a complement protein. All such scaffold or modified proteases with increased specificity and/or selectivity to any one or more complement protein are candidate therapeutics.

Where the protease exhibits an increased specificity and/or selectivity to any one or more complement protein, *in vitro* and *in vivo* assays can be used to monitor or screen proteases for effects on complement-mediated functions. Such assays are well known to those of skill in the art. One of skill in the art can test a particular scaffold or modified protease for cleavage of any one or more complement protein and/or test to assess any change in the effects of a protease on a complement-mediated activity compared to the absence of a protease. Some such assays are exemplified herein.

Exemplary *in vitro* and *in vivo* assays are provided herein for comparison of an activity of a scaffold or modified protease on the function of any one or more targeted complement proteins. Many of the assays are applicable to other proteases and modified proteases. In addition, numerous assays, such as assays for measuring complement activation, are known to one of skill in the art. Assays for activities of complement include, but are not limited to, assays that measure activation products of complement activation, such as for example the C5b-9 MAC complex, and generation of any one or more of the complement cleavage products such as C4a, C5a, C3b, and C3d. Assays to measure complement activation also include functional assays that measure the functional activity of specific components of the complement pathways, such as for example hemolytic assays used to measure activation of any one of the classical, lectin or alternative pathways. Assays to assess effects of proteases and modified proteases on complement proteins and/or complement-mediated functions include, but are not limited to, SDS-analysis followed by Western Blot or Coomassie Brilliant Blue staining, enzyme immunoassays, and hemolytic assays. In one example, *in vitro* assays can be performed using purified complement proteins. In another example, *in vivo* assays can be performed by testing the serum of a species, including mammalian or human species, for functional activation of complement. Exemplary assays are described below.

a. Protein detection

Protein detection is a means to measure individual complement components in a sample. Complement proteins can be detected to assess directly the effects of a scaffold or modified protease on cleavage of the proteins, or alternatively, complement proteins can be measured as a means to assess for complement activation. Complement proteins, treated in the presence or absence of a scaffold or modified protease, can be analyzed by any one or more assays including SDS-PAGE followed by Coomassie staining or Western Blot, enzyme immunoassay, immunohistochemistry, flow cytometry, nephelometry, agar gel diffusion, or radial immunodiffusion. Exemplary assays for protein detection are described below.

i. SDS-PAGE analysis

Analysis of complement proteins in the presence or absence of increasing concentrations of a scaffold or modified protease can be performed by analysis of proteins on SDS-PAGE followed by detection of those proteins. In such examples, complement proteins can be detected by staining for total protein, such as by Coomasie Brilliant Blue stain, Silver stain, or by any other method known to one of skill in the art, or by Western Blot using polyclonal or monoclonal antibodies specific for a specified protein. Typically, a purified complement protein, such as for example any one or more of the proteins involved in the complement pathways, can be incubated in the presence or absence of a scaffold or modified protease. The treated complement protein can be resolved on an SDS-PAGE gel followed by a method to detect protein in the gel, for example, by staining with Coomasie Brilliant blue. The treated protein can be compared to its cognate full length protein and the degradation products formed by protease cleavage of the protein can be determined.

In another embodiment, a sample, such as for example human serum or plasma, can be treated in the presence or absence of a scaffold or modified protease or can be collected after treatment of an animal or a human with or without a protease. The protease-treated sample can be analyzed on SDS-PAGE and a specific complement protein can be detected, such as for example C1q, MBL, C2, C3, C4, C5, or Factor B, by Western Blot using monoclonal or polyclonal antibodies against the protein. The cleavage of the complement protein can be compared to a sample that was not treated with a protease. Additionally, the sample can be stimulated to initiate complement activation such as by incubation with IgG which stimulates activation of the classical pathway or by LPS which stimulates activation of the alternative pathway. The sample can be resolved by SDS-PAGE for detection of any one or more of the native complement proteins to determine the presence or absence of cleavage products of a specified protein compared to a sample of the protein not treated with a protease. In such examples, cleavage effector molecules of native complement proteins also can be analyzed by Western Blot using monoclonal and polyclonal antibodies to assess the activation of one or more of the complement pathways. Examples of complement effector molecules can include, but are not limited to, C3a, C3d, iC3b, C4d, Bb, and C5-b9. For example, a decreased expression

in a sample of C4d can indicate that a scaffold or modified protease inhibited the activation of one or more of the classical or lectin pathway of complement. In another example, a decreased expression in a sample of Bb can indicate that a scaffold or modified protease inhibited the activation of the alternative pathway of complement. The cleavage products of the effector molecules also can be determined to assess the effects of increasing concentrations of a scaffold or modified protease on the cleavage of complement effector molecule themselves.

ii. Enzyme Immunoassay

Enzyme immunoassay (EIA; also called enzyme-linked immunosorbent assay; ELISA) is an assay used to measure the presence of a protein in a sample. Typically, measurement of the protein is an indirect measurement of the binding of the protein to an antibody, which itself is chemically labeled with a detectable substrate such as an enzyme or fluorescent compound. EIA assays can be used to measure the effects of scaffold or modified proteases on complement activation by measuring for the presence of a complement effector molecule generated following complement activation. In such examples, a sample, such as for example human serum or plasma, can be pretreated in the presence or absence of increasing concentrations of a scaffold or modified protease and subsequently activated to induce complement activation by incubation with initiating molecules, or can be collected following treatment of an animal or a human with a protease. For example, the classical pathway can be activated by incubation with IgG and the alternative pathway can be activated by incubation of the sample with LPS. A complement activation assay specific for the lectin pathway requires that the classical pathway of complement is inhibited since the C4/C2 cleaving activity of the lectin pathway is shared with the classical pathway of complement. Inhibition of the classical pathway can be achieved using a high ionic strength buffer which inhibits the binding of C1q to immune complexes and disrupts the C1 complex, whereas a high ionic strength buffer does not affect the carbohydrate binding activity of MBL. Consequently, activation of the lectin pathway can be induced by incubation of a sample, such as human serum or plasma, with a mannan-coated surface in the presence of 1 M NaCl.

Following activation, the sample can be quenched with the addition of Pefabloc (Roche) and EDTA to minimize continued activation of the pathways. Samples can be analyzed for the presence of complement effector molecules by an EIA or ELISA assay. EIA and ELISA assays for measuring complement proteins are well known to one skilled in the art. Any complement activation product can be assessed. Exemplary complement activation products for measurement of complement activation include iC3b, Bb, C4d, C5b-9, C3a, C3a-desArg, C4a-desArg, and C5a-desArg. The complement pathway activated can be determined depending on the complement activation product measured. For example, measurement of Bb cleavage product is a unique marker of the alternative pathway.

In some examples, the EIA can be paired with detection of the cleaved complement proteins by analysis of the protease-treated, complement-stimulated sample by SDS-PAGE followed by Western blot analysis for identification of specific complement components. Using densitometry software, the cleavage of the complement product can be compared to the full length complement component cleaved throughout the assay and the appearance of all major degradation products and the percentage cleavage can be determined.

iii. Radial Immunodiffusion (RID)

Radial immunodiffusion (RID) is a technique that relies on the precipitation of immune complexes formed between antibodies incorporated into agarose gels when it is poured, and antigen present in a test sample resulting in a circular precipitin line around the sample well. The diameter of the precipitin ring is proportional to the concentration of the antibody (or antigen) present in the test sample. By comparing the diameter of the test specimen precipitin ring to known standards, a relatively insensitive estimation of the concentration of specific antibody or antigen can be achieved. RID can be used to measure the amount of a complement protein in a sample. For example, a sample such as for example human serum or plasma, can be treated in the presence or absence of increasing concentrations of a scaffold or modified protease. The protease-treated sample can be added to a well of an agarose gel that has been made to incorporate a polyclonal or monoclonal antibody against any one of the complement proteins such as including, but not limited to, C1q, C1r,

C1s, C2, C3, C4, C5, C6, C7, C9, or Factor B. After removal of unprecipitated proteins by exposure to 0.15 M NaCl, the precipitated protein rings can be assessed by staining with a protein dye, such as for example Coomassie Brilliant blue or Crowles double stain.

b. Hemolytic assays

Functional hemolytic assays provide information on complement function as a whole. This type of assay uses antibody-sensitized or unsensitized sheep erythrocytes. Hemolytic assays include the total hemolytic complement assay (CH50), which measures the ability of the classical pathway and the MAC to lyse a sheep RBC. It depends on the sequential activation of the classical pathway components (C1 through C9) to lyse sheep erythrocytes that have been sensitized with optimal amounts of rabbit anti-sheep erythrocyte antibodies to make cellular antigen-antibody complexes. Hemolytic assays also can include an alternative pathway CH50 assay (rabbit CH50 or APCH50), which measures the ability of the alternative pathway and the MAC to lyse a rabbit RBC. One CH50 and/or APCH50 unit is defined as the quantity or dilution of serum required to lyse 50% of the red cells in the test. Typically, to assess complement activation, a sample, such as for example human serum or human plasma, can be treated in the presence or absence of increasing concentrations of a scaffold or modified protease, or can be collected following treatment of an animal or human in the presence or absence of a protease. The protease-treated sample can be subsequently mixed with sheep's red blood cells that have been activated or sensitized with IgG. A water only sample mixed with sheep red blood cells can act as a total lysis control in order to accurately assess percent lysis of the samples analyzed. The addition of 0.15M NaCl to the sample can be added to stop the lysing reaction. Lysis of the red blood cells, induced by the activation of the terminal components of the complement pathway, can be assessed by measuring the release of hemoglobin. Measurement can be by optical density (OD) readings of the samples using a spectrophotometer at an OD of 415 nm.

In one embodiment, limiting dilution hemolytic assays can be used to measure functional activity of specific components of either pathway. In such an assay, a serum source is used that has an excess of all complement components, but is

deficient for the one being measured in the sample, *i.e.* a media or serum source is complement-depleted for a specific protein. The extent of hemolysis is therefore dependent on the presence of the measured component in the test sample. In such an assay, a purified complement protein, such as for example any one of the native complement proteins including, but not limited to C1q, MBL, C2, C3, C4, or C5 can be incubated in the presence or absence of increasing concentrations of a scaffold or modified protease. The protease-treated purified complement protein can then be mixed with complement-depleted media or plasma and IgG-activated sheep red blood cells and hemolysis of the sample can be assessed as described above. In another embodiment, protease cleavage can be correlated with complement activation by assaying for hemolytic activity of a protease-treated sample, and subsequently analyzing the sample on SDS-PAGE gel followed by staining with a protein stain, such as for example Coomassie Blue. The purified complement protein treated with the proteases can be assessed for cleavage and the percentage of the full length complement component cleaved throughout the assay and the appearance of all major degradation products can be calculated. Alternatively, analysis of the protease-treated complement protein can be by Western blot.

An alternative to the hemolytic assay, called the liposome immunoassay (LIA), can be used to assess activation of the classical pathway. The LIA (Waco Chemicals USA, Richmond, Va.) utilizes dinitrophenyl (DNP)-coated liposomes that contain the enzyme glucose-6-phosphate dehydrogenase. When serum is mixed with the liposomes and a substrate containing anti-DNP antibody, glucose-6-phosphate, and nicotinamide adenine dinucleotide, activated liposomes lyse, and an enzymatic colorimetric reaction occurs which is proportional to total classical complement activity.

F. Methods of Producing Nucleic Acid Encoding Proteases and Methods of Producing Protease Polypeptides

Protease polypeptides, including modified MT-SP1 polypeptides, or domains thereof, can be obtained by methods well known in the art for protein purification and recombinant protein expression. Any method known to those of skill in the art for identification of nucleic acids that encode desired genes can be used. Any method

available in the art can be used to obtain a full length (*i.e.*, encompassing the entire coding region) cDNA or genomic DNA clone encoding a protease protein, such as from a cell or tissue source. Modified proteases can be engineered as described herein from a scaffold or wildtype protease, such as by site-directed mutagenesis.

Proteases can be cloned or isolated using any available methods known in the art for cloning and isolating nucleic acid molecules. Such methods include PCR amplification of nucleic acids and screening of libraries, including nucleic acid hybridization screening, antibody-based screening and activity-based screening.

Methods for amplification of nucleic acids can be used to isolate nucleic acid molecules encoding a protease, including for example, polymerase chain reaction (PCR) methods. A nucleic acid containing material can be used as a starting material from which a protease-encoding nucleic acid molecule can be isolated. For example, DNA and mRNA preparations, cell extracts, tissue extracts, fluid samples (*e.g.* blood, serum, saliva), samples from healthy and/or diseased subjects can be used in amplification methods. Nucleic acid libraries also can be used as a source of starting material. Primers can be designed to amplify a protease. For example, primers can be designed based on expressed sequences from which a protease is generated. Primers can be designed based on back-translation of a protease amino acid sequence. Nucleic acid molecules generated by amplification can be sequenced and confirmed to encode a protease.

Additional nucleotide sequences can be joined to a protease-encoding nucleic acid molecule, including linker sequences containing restriction endonuclease sites for the purpose of cloning the synthetic gene into a vector, for example, a protein expression vector or a vector designed for the amplification of the core protein coding DNA sequences. Furthermore, additional nucleotide sequences specifying functional DNA elements can be operatively linked to a protease-encoding nucleic acid molecule. Examples of such sequences include, but are not limited to, promoter sequences designed to facilitate intracellular protein expression, and secretion sequences designed to facilitate protein secretion. Additional nucleotide sequences such as sequences specifying protein binding regions also can be linked to protease-encoding nucleic acid molecules. Such regions include, but are not limited to,

sequences to facilitate uptake of a protease into specific target cells, or otherwise enhance the pharmacokinetics of the synthetic gene.

The identified and isolated nucleic acids can then be inserted into an appropriate cloning vector. A large number of vector-host systems known in the art can be used. Possible vectors include, but are not limited to, plasmids or modified viruses, but the vector system must be compatible with the host cell used. Such vectors include, but are not limited to, bacteriophages such as lambda derivatives, or plasmids such as pBR322 or pUC plasmid derivatives or the Bluescript vector (Stratagene, La Jolla, CA). The insertion into a cloning vector can, for example, be accomplished by ligating the DNA fragment into a cloning vector which has complementary cohesive termini. Insertion can be effected using TOPO cloning vectors (INVITROGEN, Carlsbad, CA). If the complementary restriction sites used to fragment the DNA are not present in the cloning vector, the ends of the DNA molecules can be enzymatically modified. Alternatively, any site desired can be produced by ligating nucleotide sequences (linkers) onto the DNA termini; these ligated linkers can contain specific chemically synthesized oligonucleotides encoding restriction endonuclease recognition sequences. In an alternative method, the cleaved vector and protease protein gene can be modified by homopolymeric tailing. Recombinant molecules can be introduced into host cells via, for example, transformation, transfection, infection, electroporation and sonoporation, so that many copies of the gene sequence are generated.

In specific embodiments, transformation of host cells with recombinant DNA molecules that incorporate the isolated protease protein gene, cDNA, or synthesized DNA sequence enables generation of multiple copies of the gene. Thus, the gene can be obtained in large quantities by growing transformants, isolating the recombinant DNA molecules from the transformants and, when necessary, retrieving the inserted gene from the isolated recombinant DNA.

1. Vectors and cells

For recombinant expression of one or more of the protease proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protease protein can be inserted into an appropriate expression vector, *i.e.*, a vector

that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals also can be supplied by the native promoter for protease genes, and/or their flanking regions.

Also provided are vectors that contain nucleic acid encoding the protease or modified protease. Cells containing the vectors also are provided. The cells include eukaryotic and prokaryotic cells, and the vectors are any suitable for use therein.

Prokaryotic and eukaryotic cells, including endothelial cells, containing the vectors are provided. Such cells include bacterial cells, yeast cells, fungal cells, Archea, plant cells, insect cells and animal cells. The cells are used to produce a protease or modified protease protein thereof by growing the above-described cells under conditions whereby the encoded protease protein is expressed by the cell, and recovering the expressed protease protein. For purposes herein, the protease can be secreted into the medium.

In one embodiment, vectors containing a sequence of nucleotides that encodes a polypeptide that has protease activity and contains all or a portion of the protease domain, or multiple copies thereof, are provided. Also provided are vectors that contain a sequence of nucleotides that encodes the protease domain and additional portions of a protease protein up to and including a full length protease protein, as well as multiple copies thereof. The vectors can be selected for expression of the scaffold or modified protease protein or protease domain thereof in the cell or such that the protease protein is expressed as a secreted protein. When the protease domain is expressed the nucleic acid is linked to nucleic acid encoding a secretion signal, such as the *Saccharomyces cerevisiae* α-mating factor signal sequence or a portion thereof, or the native signal sequence.

A variety of host-vector systems can be used to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (*e.g.* vaccinia virus, adenovirus and other viruses); insect cell systems infected with virus (*e.g.* baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities.

Depending on the host-vector system used, any one of a number of suitable transcription and translation elements can be used.

Any methods known to those of skill in the art for the insertion of DNA fragments into a vector can be used to construct expression vectors containing a chimeric gene containing appropriate transcriptional/translational control signals and protein coding sequences. These methods can include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinants (genetic recombination). Expression of nucleic acid sequences encoding a scaffold or modified protease protein, or domains, derivatives, fragments or homologs thereof, can be regulated by a second nucleic acid sequence so that the genes or fragments thereof are expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins can be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the genes for a protease protein. Promoters which can be used include but are not limited to the SV40 early promoter (Bernoist and Chambon, *Nature 290*:304-310 (1981)), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto *et al. Cell 22*:787-797 (1980)), the herpes thymidine kinase promoter (Wagner *et al.*, *Proc. Natl. Acad. Sci. USA 78*:1441-1445 (1981)), the regulatory sequences of the metallothionein gene (Brinster *et al.*, *Nature 296*:39-42 (1982)); prokaryotic expression vectors such as the β-lactamase promoter (Jay *et al.*, (1981) *Proc. Natl. Acad. Sci. USA 78*:5543) or the *tac* promoter (DeBoer *et al.*, *Proc. Natl. Acad. Sci. USA 80*:21-25 (1983)); see also "Useful Proteins from Recombinant Bacteria": in Scientific American *242*:79-94 (1980)); plant expression vectors containing the nopaline synthetase promoter (Herrar-Estrella *et al.*, *Nature 303*:209-213 (1984)) or the cauliflower mosaic virus 35S RNA promoter (Garder *et al.*, *Nucleic Acids Res. 9*:2871 (1981)), and the promoter of the photosynthetic enzyme ribulose bisphosphate carboxylase (Herrera-Estrella *et al.*, *Nature 310*:115-120 (1984)); promoter elements from yeast and other fungi such as the Gal4 promoter, the alcohol dehydrogenase promoter, the phosphoglycerol kinase promoter, the alkaline phosphatase promoter, and the following animal transcriptional control regions that exhibit tissue specificity and have been used in transgenic animals: elastase I gene control region which is active in pancreatic acinar cells (Swift *et al.*, *Cell 38*:639-646

(1984); Ornitz *et al.*, *Cold Spring Harbor Symp. Quant. Biol. 50*:399-409 (1986); MacDonald, *Hepatology 7*:425-515 (1987)); insulin gene control region which is active in pancreatic beta cells (Hanahan *et al.*, *Nature 315*:115-122 (1985)), immunoglobulin gene control region which is active in lymphoid cells (Grosschedl *et al.*, *Cell 38*:647-658 (1984); Adams *et al.*, *Nature 318*:533-538 (1985); Alexander *et al.*, *Mol. Cell Biol. 7*:1436-1444 (1987)), mouse mammary tumor virus control region which is active in testicular, breast, lymphoid and mast cells (Leder *et al.*, *Cell 45*:485-495 (1986)), albumin gene control region which is active in liver (Pinckert *et al.*, *Genes and Devel. 1*:268-276 (1987)), alpha-fetoprotein gene control region which is active in liver (Krumlauf *et al.*, *Mol. Cell. Biol. 5*:1639-1648 (1985); Hammer *et al.*, *Science 235*:53-58 1987)), alpha-1 antitrypsin gene control region which is active in liver (Kelsey *et al.*, *Genes and Devel. 1*:161-171 (1987)), beta globin gene control region which is active in myeloid cells (Mogram *et al.*, *Nature 315*:338-340 (1985); Kollias *et al.*, *Cell 46*:89-94 (1986)), myelin basic protein gene control region which is active in oligodendrocyte cells of the brain (Readhead *et al.*, *Cell 48*:703-712 (1987)), myosin light chain-2 gene control region which is active in skeletal muscle (Sani, *Nature 314*:283-286 (1985)), and gonadotrophic releasing hormone gene control region which is active in gonadotrophs of the hypothalamus (Mason *et al.*, *Science 234*:1372-1378 (1986)).

In a specific embodiment, a vector is used that contains a promoter operably linked to nucleic acids encoding a scaffold or modified protease protein, or a domain, fragment, derivative or homolog, thereof, one or more origins of replication, and optionally, one or more selectable markers (*e.g.*, an antibiotic resistance gene). Vectors and systems for expression of the protease domains of the protease proteins include the well known *Pichia* vectors (available, for example, from Invitrogen, San Diego, CA), particularly those designed for secretion of the encoded proteins. Exemplary plasmid vectors for transformation of *E.coli* cells, include, for example, the pQE expression vectors (available from Qiagen, Valencia, CA; see also literature published by Qiagen describing the system). pQE vectors have a phage T5 promoter (recognized by *E. coli* RNA polymerase) and a double lac operator repression module to provide tightly regulated, high-level expression of recombinant proteins in *E. coli*,

a synthetic ribosomal binding site (RBS II) for efficient translation, a 6XHis tag coding sequence, t_0 and T1 transcriptional terminators, ColE1 origin of replication, and a beta-lactamase gene for conferring ampicillin resistance. The pQE vectors enable placement of a 6xHis tag at either the N- or C-terminus of the recombinant protein. Such plasmids include pQE 32 (SEQ ID NO: 345), pQE 30, and pQE 31 which provide multiple cloning sites for all three reading frames and provide for the expression of N-terminally 6xHis-tagged proteins. Other exemplary plasmid vectors for transformation of *E. coli* cells, include, for example, the pET expression vectors (see, U.S patent 4,952,496; available from NOVAGEN, Madison, WI; see, also literature published by Novagen describing the system). Such plasmids include pET 11a, which contains the T7lac promoter, T7 terminator, the inducible *E. coli* lac operator, and the lac repressor gene; pET 12a-c, which contains the T7 promoter, T7 terminator, and the *E. coli* ompT secretion signal; and pET 15b and pET19b (NOVAGEN, Madison, WI), which contain a His-Tag™ leader sequence for use in purification with a His column and a thrombin cleavage site that permits cleavage following purification over the column, the T7-lac promoter region and the T7 terminator.

2. Expression

Modified proteases can be produced by any method known to those of skill in the art including *in vivo* and *in vitro* methods. Modified proteases can be expressed in any organism suitable to produce the required amounts and forms of a modified protease needed for administration and treatment. Expression hosts include prokaryotic and eukaryotic organisms such as *E.coli*, yeast, plants, insect cells, mammalian cells, including human cell lines and transgenic animals. Expression hosts can differ in their protein production levels as well as the types of post-translational modifications that are present on the expressed proteins. The choice of expression host can be made based on these and other factors, such as regulatory and safety considerations, production costs and the need and methods for purification.

Many expression vectors are available and known to those of skill in the art and can be used for expression of modified proteases. The choice of expression vector will be influenced by the choice of host expression system. In general,

expression vectors can include transcriptional promoters and optionally enhancers, translational signals, and transcriptional and translational termination signals. Expression vectors that are used for stable transformation typically have a selectable marker which allows selection and maintenance of the transformed cells. In some cases, an origin of replication can be used to amplify the copy number of the vector.

Modified proteases also can be utilized or expressed as protein fusions. For example, a protease fusion can be generated to add additional functionality to a protease. Examples of protease fusion proteins include, but are not limited to, fusions of a signal sequence, a tag such as for localization, *e.g.* a his_6 tag or a myc tag, or a tag for purification, for example, a GST fusion, and a sequence for directing protein secretion and/or membrane association.

In one embodiment, the protease can be expressed in an active form. In another embodiment, the protease is expressed in an inactive, zymogen form.

a. Prokaryotes

Prokaryotes, especially *E.coli*, provide a system for producing large amounts of proteins such as proteases or modified proteases. Transformation of *E.coli* is simple and rapid technique well known to those of skill in the art. Expression vectors for *E.coli* can contain inducible promoters, such promoters are useful for inducing high levels of protein expression and for expressing proteins that exhibit some toxicity to the host cells. Examples of inducible promoters include the lac promoter, the trp promoter, the hybrid tac promoter, the T7 and SP6 RNA promoters and the temperature regulated λPL promoter.

Modified proteases can be expressed in the cytoplasmic environment of *E.coli*. The cytoplasm is a reducing environment and for some molecules, this can result in the formation of insoluble inclusion bodies. Reducing agents such as dithiothreotol and β-mercaptoethanol and denaturants, such as guanidine-HCl and urea can be used to resolubilize the proteins. An alternative approach is the expression of a modified protease in the periplasmic space of bacteria which provides an oxidizing environment and chaperonin-like and disulfide isomerases and can lead to the production of soluble protein. Typically, a leader sequence is fused to the protein to be expressed which directs the protein to the periplasm. The leader is then removed

by signal peptidases inside the periplasm. Examples of periplasmic-targeting leader sequences include the pelB leader from the pectate lyase gene and the leader derived from the alkaline phosphatase gene. In some cases, periplasmic expression allows leakage of the expressed protein into the culture medium. The secretion of proteins allows quick and simple purification from the culture supernatant. Proteins that are not secreted can be obtained from the periplasm by osmotic lysis. Similar to cytoplasmic expression, in some cases proteins can become insoluble and denaturants and reducing agents can be used to facilitate solubilization and refolding. Temperature of induction and growth also can influence expression levels and solubility, typically temperatures between 25°C and 37°C are used. Typically, bacteria produce aglycosylated proteins. Thus, if proteins require glycosylation for function, glycosylation can be added *in vitro* after purification from host cells.

b. Yeast

Yeasts such as *Saccharomyces cerevisae, Schizosaccharomyces pombe, Yarrowia lipolytica, Kluyveromyces lactis* and *Pichia pastoris* are well known yeast expression hosts that can be used for production of modified proteases. Yeast can be transformed with episomal replicating vectors or by stable chromosomal integration by homologous recombination. Typically, inducible promoters are used to regulate gene expression. Examples of such promoters include GAL1, GAL7 and GAL5 and metallothionein promoters, such as CUP1, AOX1 or other *Pichia* or other yeast promoter. Expression vectors often include a selectable marker such as LEU2, TRP1, HIS3 and URA3 for selection and maintenance of the transformed DNA. Proteins expressed in yeast are often soluble. Co-expression with chaperonins such as Bip and protein disulfide isomerase can improve expression levels and solubility. Additionally, proteins expressed in yeast can be directed for secretion using secretion signal peptide fusions such as the yeast mating type alpha-factor secretion signal from *Saccharomyces cerevisae* and fusions with yeast cell surface proteins such as the Aga2p mating adhesion receptor or the *Arxula adeninivorans* glucoamylase. A protease cleavage site such as for the Kex-2 protease, can be engineered to remove the fused sequences from the expressed polypeptides as they exit the secretion pathway. Yeast also is capable of glycosylation at Asn-X-Ser/Thr motifs.

c. Insect cells

Insect cells, particularly using baculovirus expression, are useful for expressing polypeptides such as modified proteases. Insect cells express high levels of protein and are capable of most of the post-translational modifications used by higher eukaryotes. Baculovirus have a restrictive host range which improves the safety and reduces regulatory concerns of eukaryotic expression. Typical expression vectors use a promoter for high level expression such as the polyhedrin promoter of baculovirus. Commonly used baculovirus systems include the baculoviruses such as *Autographa californica* nuclear polyhedrosis virus (AcNPV), and the *Bombyx mori* nuclear polyhedrosis virus (BmNPV) and an insect cell line such as Sf9 derived from *Spodoptera frugiperda, Pseudaletia unipuncta* (A7S) and *Danaus plexippus* (DpN1). For high-level expression, the nucleotide sequence of the molecule to be expressed is fused immediately downstream of the polyhedrin initiation codon of the virus. Mammalian secretion signals are accurately processed in insect cells and can be used to secrete the expressed protein into the culture medium. In addition, the cell lines *Pseudaletia unipuncta* (A7S) and *Danaus plexippus* (DpN1) produce proteins with glycosylation patterns similar to mammalian cell systems.

An alternative expression system in insect cells is the use of stably transformed cells. Cell lines such as the Schnieder 2 (S2) and Kc cells (*Drosophila melanogaster*) and C7 cells (*Aedes albopictus*) can be used for expression. The *Drosophila* metallothionein promoter can be used to induce high levels of expression in the presence of heavy metal induction with cadmium or copper. Expression vectors are typically maintained by the use of selectable markers such as neomycin and hygromycin.

d. Mammalian cells

Mammalian expression systems can be used to express modified proteases. Expression constructs can be transferred to mammalian cells by viral infection such as adenovirus or by direct DNA transfer such as liposomes, calcium phosphate, DEAE-dextran and by physical means such as electroporation and microinjection. Expression vectors for mammalian cells typically include an mRNA cap site, a TATA box, a translational initiation sequence (Kozak consensus sequence) and

polyadenylation elements. Such vectors often include transcriptional promoter-enhancers for high-level expression, for example the SV40 promoter-enhancer, the human cytomegalovirus (CMV) promoter and the long terminal repeat of Rous sarcoma virus (RSV). These promoter-enhancers are active in many cell types. Tissue and cell-type promoters and enhancer regions also can be used for expression. Exemplary promoter/enhancer regions include, but are not limited to, those from genes such as elastase I, insulin, immunoglobulin, mouse mammary tumor virus, albumin, alpha fetoprotein, alpha-1 antitrypsin, beta globin, myelin basic protein, myosin light chain 2, and gonadotropic releasing hormone gene control. Selectable markers can be used to select for and maintain cells with the expression construct. Examples of selectable marker genes include, but are not limited to, hygromycin B phosphotransferase, adenosine deaminase, xanthine-guanine phosphoribosyl transferase, aminoglycoside phosphotransferase, dihydrofolate reductase and thymidine kinase. Fusion with cell surface signaling molecules such as TCR-ζ and $Fc_{\varepsilon}RI$-γ can direct expression of the proteins in an active state on the cell surface.

Many cell lines are available for mammalian expression including mouse, rat human, monkey, chicken and hamster cells. Exemplary cell lines include, but are not limited to, CHO, Balb/3T3, HeLa, MT2, mouse NS0 (nonsecreting) and other myeloma cell lines, hybridoma and heterohybridoma cell lines, lymphocytes, fibroblasts, Sp2/0, COS, NIH3T3, HEK293, 293S, 2B8, and HKB cells. Cell lines also are available adapted to serum-free media which facilitates purification of secreted proteins from the cell culture media. One such example is the serum free EBNA-1 cell line (Pham *et al.*, (2003) *Biotechnol. Bioeng. 84*:332-42.)

e. Plants

Transgenic plant cells and plants can be to express modified proteases. Expression constructs are typically transferred to plants using direct DNA transfer such as microprojectile bombardment and PEG-mediated transfer into protoplasts, and with agrobacterium-mediated transformation. Expression vectors can include promoter and enhancer sequences, transcriptional termination elements and translational control elements. Expression vectors and transformation techniques are usually divided between dicot hosts, such as *Arabidopsis* and tobacco, and monocot

hosts, such as corn and rice. Examples of plant promoters used for expression include the cauliflower mosaic virus promoter, the nopaline synthase promoter, the ribose bisphosphate carboxylase promoter and the ubiquitin and UBQ3 promoters. Selectable markers such as hygromycin, phosphomannose isomerase and neomycin phosphotransferase are often used to facilitate selection and maintenance of transformed cells. Transformed plant cells can be maintained in culture as cells, aggregates (callus tissue) or regenerated into whole plants. Transgenic plant cells also can include algae engineered to produce proteases or modified proteases (see for example, Mayfield *et al.* (2003) *PNAS 100*:438-442). Because plants have different glycosylation patterns than mammalian cells, this can influence the choice of proteases or modified proteases produced in these hosts.

3. Purification Techniques

Methods for purification of protease polypeptides from host cells will depend on the chosen host cells and expression systems. For secreted molecules, proteins are generally purified from the culture media after removing the cells. For intracellular expression, cells can be lysed and the proteins purified from the extract. When transgenic organisms such as transgenic plants and animals are used for expression, tissues or organs can be used as starting material to make a lysed cell extract. Additionally, transgenic animal production can include the production of polypeptides in milk or eggs, which can be collected, and if necessary the proteins can be extracted and further purified using standard methods in the art.

The protease can be expressed and purified to be in an inactive form (zymogen form) or alternatively the expressed protease can be purified into an active form by autocatalysis to remove the proregion. Typically, the autoactivation occurs during the purification process, such as by incubating at room temperature for 24-72 hours. The rate and degree of activation is dependent on protein concentration and the specific modified protease, such that for example, a more dilute sample can need to be incubated at room temperature for a longer period of time. Activation can be monitored by SDS-PAGE (a 3 kilodalton shift) and by enzyme activity (cleavage of a fluorogenic substrate). Typically, a protease is allowed to achieve >75% activation before purification.

Proteases can be purified using standard protein purification techniques known in the art including, but not limited to, SDS-PAGE, size fraction and size exclusion chromatography, ammonium sulfate precipitation and ionic exchange chromatography, such as anion exchange. Affinity purification techniques also can be utilized to improve the efficiency and purity of the preparations. For example, antibodies, receptors and other molecules that bind proteases can be used in affinity purification. Expression constructs also can be engineered to add an affinity tag to a protein such as a myc epitope, GST fusion or His_6 and affinity purified with myc antibody, glutathione resin and Ni-resin, respectively. Purity can be assessed by any method known in the art including gel electrophoresis and staining and spectrophotometric techniques.

4. Fusion proteases

Fusion proteins containing a protease and one or more other polypeptides also are provided. Pharmaceutical compositions containing such fusion proteins formulated for administration by a suitable route are provided. Fusion proteins are formed by linking in any order the scaffold or modified protease and another polypeptide, such as an antibody or fragment thereof, growth factor, receptor, ligand and other such agent for the purposes of facilitating the purification of a protease, altering the pharmacodynamic properties of a protease by directing the protease to a targeted cell or tissue, and/or increasing the expression or secretion of a protease. Within a protease fusion protein, the protease polypeptide can correspond to all or a catalytically active portion thereof of a wildtype or scaffold protease protein. In some embodiments, the protease or catalytically active portion thereof is a modified protease. Fusion proteins provided herein retain substantially all of their specificity and/or selectivity for any one or more of the complement proteins. Generally, protease fusion polypeptides retain at least about 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90% or 95% substrate specificity and/or selectivity compared with a non-fusion protease, including 96%, 97%, 98%, 99% or greater substrate specificity compared with a non-fusion protease.

Linkage of a protease polypeptide and another polypeptide can be effected directly or indirectly via a linker. In one example, linkage can be by chemical

linkage, such as via heterobifunctional agents or thiol linkages or other such linkages. Fusion of a protease to another polypeptide can be to the N- or C- terminus of the protease polypeptide. Non-limiting examples of polypeptides that can be used in fusion proteins with a protease provided herein include, for example, a GST (glutathione S-transferase) polypeptide, Fc domain from immunoglobulin G, or a heterologous signal sequence. The fusion proteins can contain additional components, such as *E. coli* maltose binding protein (MBP) that aid in uptake of the protein by cells (*see*, International PCT application No. WO 01/32711).

A protease fusion protein can be produced by standard recombinant techniques. For example, DNA fragments coding for the different polypeptide sequences can be ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, *e.g.*, Ausubel *et al.* (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A protease-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protease protein.

5. Nucleotide sequences

Nucleic acid molecules encoding scaffold or modified proteases are provided herein. Nucleic acid molecules include allelic variants or splice variants of any encoded scaffold protease, or catalytically active portion thereof. In one embodiment, nucleic acid molecules provided herein have at least 50, 60, 65, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, or 99% sequence identity or hybridize under conditions of medium or high stringency along at least 70% of the full-length of any nucleic acid encoded

scaffold protease, or catalytically active portion thereof. In another embodiment, a nucleic acid molecule can include those with degenerate codon sequences of any of the scaffold proteases or catalytically active portions thereof such as those provided herein. Exemplary nucleic acid molecules, encoding scaffold or modified proteases, or catalytically active portions thereof, have a sequence of nucleotides as set forth in any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 451-523, and 534-543.

Nucleic acid molecules, or fusion proteins containing a catalytically active portion of a nucleic acid molecule, operably-linked to a promoter, such as an inducible promoter for expression in mammalian cells also are provided. Such promoters include, but are not limited to, CMV and SV40 promoters; adenovirus promoters, such as the E2 gene promoter, which is responsive to the HPV E7 oncoprotein; a PV promoter, such as the PBV p89 promoter that is responsive to the PV E2 protein; and other promoters that are activated by the HIV or PV or oncogenes.

Scaffold or modified proteases provided herein, also can be delivered to the cells in gene transfer vectors. The transfer vectors also can encode additional other therapeutic agent(s) for treatment of the disease or disorder, such as Rheumatoid Arthritis or cardiovascular disease, for which the protease is administered. Transfer vectors encoding a protease can be used systemically, by administering the nucleic acid to a subject. For example, the transfer vector can be a viral vector, such as an adenovirus vector. Vectors encoding a protease also can be incorporated into stem cells and such stem cells administered to a subject such as by transplanting or engrafting the stem cells at sites for therapy. For example, mesenchymal stem cells (MSCs) can be engineered to express a protease and such MSCs engrafted at a tumor site for therapy.

G. METHODS OF USING: Formulation/Packaging/Administration

Pharmaceutical compositions containing a protease or modified protease produced herein, including MT-SP1 (modified) polypeptides, modified protease fusion proteins or encoding nucleic acid molecules, can be formulated in any conventional manner by mixing a selected amount of the polypeptide with one or more physiologically acceptable carriers or excipients. Selection of the carrier or

excipient is within the skill of the administering profession and can depend upon a number of parameters. These include, for example, the mode of administration (*i.e.*, systemic, oral, nasal, pulmonary, local, topical or any other mode) and disorder treated. The pharmaceutical compositions provided herein can be formulated for single dosage (direct) administration or for dilution or other modification. The concentrations of the compounds in the formulations are effective for delivery of an amount, upon administration, that is effective for the intended treatment. Typically, the compositions are formulated for single dosage administration. To formulate a composition, the weight fraction of a compound or mixture thereof is dissolved, suspended, dispersed or otherwise mixed in a selected vehicle at an effective concentration such that the treated condition is relieved or ameliorated. Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration.

1. Administration of modified protease polypeptides

The polypeptides can be formulated as the sole pharmaceutically active ingredient in the composition or can be combined with other active ingredients. The polypeptides can be targeted for delivery, such as by conjugation to a targeting agent, such as an antibody. Liposomal suspensions, including tissue-targeted liposomes, also can be suitable as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art. For example, liposome formulations can be prepared as described in U.S. Patent No. 4,522,811. Liposomal delivery also can include slow release formulations, including pharmaceutical matrices such as collagen gels and liposomes modified with fibronectin (*see*, for example, Weiner et al. (1985) *J Pharm Sci.* 74(9): 922-5).

The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the subject treated. The therapeutically effective concentration can be determined empirically by testing the compounds in known *in vitro* and *in vivo* systems, such as the assays provided herein.

The polypeptides provided herein (*i.e.* active compounds) can be administered *in vitro*, *ex vivo*, or *in vivo* by contacting a mixture, such as a body fluid or other tissue sample, with a protease polypeptide provided herein, including any of the modified MT-SP1 proteases provided herein. For example, when administering a compound *ex vivo*, a body fluid or tissue sample from a subject can be contacted with the protease polypeptides that are coated on a tube or filter, such as for example, a tube or filter in a bypass machine. When administering *in vivo*, the active compounds can be administered by any appropriate route, for example, orally, nasally, pulmonary, parenterally, intravenously, intradermally, subcutaneously, or topically, in liquid, semi-liquid or solid form and are formulated in a manner suitable for each route of administration.

The modified protease and physiologically acceptable salts and solvates can be formulated for administration by inhalation (either through the mouth or the nose), oral, transdermal, pulmonary, parenteral or rectal administration. For administration by inhalation, the modified protease can be delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit can be determined by providing a valve to deliver a metered amount. Capsules and cartridges of *e.g.*, gelatin for use in an inhaler or insufflator, can be formulated containing a powder mix of a therapeutic compound and a suitable powder base such as lactose or starch.

For pulmonary administration to the lungs, the modified protease can be delivered in the form of an aerosol spray presentation from a nebulizer, turbonebulizer, or microprocessor-controlled metered dose oral inhaler with the use of a suitable propellant. Generally, particle size of the aerosol is small, such as in the range of 0.5 to 5 microns. In the case of a pharmaceutical composition formulated for pulmonary administration, detergent surfactants are not typically used. Pulmonary drug delivery is a promising non-invasive method of systemic administration. The lungs represent an attractive route for drug delivery, mainly due to the high surface

area for absorption, thin alveolar epithelium, extensive vascularization, lack of hepatic first-pass metabolism, and relatively low metabolic activity.

For oral administration, the pharmaceutical compositions can take the form of, for example, tablets, pills, liquid suspensions, or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (*e.g.*, pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (*e.g.*, lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (*e.g.*, potato starch or sodium starch glycolate); or wetting agents (*e.g.*, sodium lauryl sulphate). The tablets can be coated by methods well known in the art. Liquid preparations for oral administration can take the form of, for example, solutions, syrups or suspensions, or they can be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations can be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (*e.g.*, sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (*e.g.*, lecithin or acacia); non-aqueous vehicles (*e.g.*, almond oil, oily esters, ethyl alcohol or fractionated vegetable oils); and preservatives (*e.g.*, methyl or propyl-p-hydroxybenzoates or sorbic acid). The preparations also can contain buffer salts, flavoring, coloring and sweetening agents as appropriate.

Preparations for oral administration can be formulated for controlled release of the active compound. For buccal administration the compositions can take the form of tablets or lozenges formulated in conventional manner.

The modified protease polypeptides can be formulated as a depot preparation. Such long-acting formulations can be administered by implantation (for example, subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the therapeutic compounds can be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

The modified protease can be formulated for parenteral administration by injection (*e.g.*, by bolus injection or continuous infusion). Formulations for injection can be presented in unit dosage form (*e.g.*, in ampoules or in multi-dose containers)

with an added preservative. The compositions can take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles and can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient can be in powder-lyophilized form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The pharmaceutical compositions can be formulated for local or topical application, such as for topical application to the skin (transdermal) and mucous membranes, such as in the eye, in the form of gels, creams, and lotions and for application to the eye or for intracisternal or intraspinal application. Such solutions, particularly those intended for ophthalmic use, can be formulated as 0.01% - 10% isotonic solutions and pH about 5-7 with appropriate salts. The compounds can be formulated as aerosols for topical application, such as by inhalation (*see*, for example, U.S. Patent Nos. 4,044,126, 4,414,209 and 4,364,923, which describe aerosols for delivery of a steroid useful for treatment inflammatory diseases, particularly asthma).

The concentration of active compound in the drug composition depends on absorption, inactivation and excretion rates of the active compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art. As described further herein, dosages can be determined empirically using comparisons of properties and activities (*e.g.*, cleavage of one or more complement proteins) of the modified protease compared to the unmodified and/or native protease.

The compositions, if desired, can be presented in a package, in a kit or dispenser device, that can contain one or more unit dosage forms containing the active ingredient. In some examples, the composition can be coated on a device, such as for example on a tube or filter in, for example, a bypass machine. The package, for example, contains metal or plastic foil, such as a blister pack. The pack or dispenser device can be accompanied by instructions for administration. The compositions containing the active agents can be packaged as articles of manufacture containing packaging material, an agent provided herein, and a label that indicates the disorder for which the agent is provided.

Also provided are compositions of nucleic acid molecules encoding the protease polypeptides and expression vectors encoding them that are suitable for gene

therapy. Rather than deliver the protein, nucleic acid can be administered *in vivo*, such as systemically or by other route, or *ex vivo*, such as by removal of cells, including lymphocytes, introduction of the nucleic therein, and reintroduction into the host or a compatible recipient.

2. Administration of nucleic acids encoding modified protease polypeptides (gene therapy)

Protease polypeptides can be delivered to cells and tissues by expression of nucleic acid molecules. Protease polypeptides can be administered as nucleic acid molecules encoding protease polypeptides, including *ex vivo* techniques and direct *in vivo* expression. Nucleic acids can be delivered to cells and tissues by any method known to those of skill in the art. The isolated nucleic acid can be incorporated into vectors for further manipulation. Exemplary nucleic acids are any that encode or that hybridize under medium to high stringency to a nucleic acid that encodes a scaffold or modified protease, or catalytically active portion thereof having a sequence of amino acids set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710. Exemplary nucleic acid molecules, encoding scaffold or modified proteases, or catalytically active portions thereof, have a sequence of nucleotides as set forth in any of SEQ ID NOS: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 451-523, and 534-543.

Methods for administering protease polypeptides by expression of encoding nucleic acid molecules include administration of recombinant vectors. The vector can be designed to remain episomal, such as by inclusion of an origin of replication or can be designed to integrate into a chromosome in the cell. Protease polypeptides also can be used in *ex vivo* gene expression therapy using vectors. For example, cells can be engineered to express a protease polypeptide, such as by integrating a protease polypeptide encoding-nucleic acid into a genomic location, either operatively linked to regulatory sequences or such that it is placed operatively linked to regulatory sequences in a genomic location. Such cells then can be administered locally or systemically to a subject, such as a patient in need of treatment. Exemplary vectors for *in vivo* and *ex vivo* gene therapy include viral vectors, and non-viral vectors such as for example, liposomes or artificial chromosomes.

Viral vectors, including, for example adenoviruses, herpes viruses, retroviruses EBV, SV40, cytomegalovirus vector, vaccinia virus vector, and others designed for gene therapy can be employed. The vectors can remain episomal or can integrate into chromosomes of the treated subject. A protease polypeptide can be expressed by a virus, which is administered to a subject in need of treatment. Virus vectors suitable for gene therapy include adenovirus, adeno-associated virus, retroviruses, lentiviruses and others noted above. For example, adenovirus expression technology is well-known in the art and adenovirus production and administration methods also are well known. Adenovirus serotypes are available, for example, from the American Type Culture Collection (ATCC, Rockville, MD). Adenovirus can be used *ex vivo*, for example, cells are isolated from a patient in need of treatment, and transduced with a protease polypeptide-expressing adenovirus vector. After a suitable culturing period, the transduced cells are administered to a subject, locally and/or systemically. Alternatively, protease polypeptide-expressing adenovirus particles are isolated and formulated in a pharmaceutically-acceptable carrier for delivery of a therapeutically effective amount to prevent, treat or ameliorate a disease or condition of a subject. In one embodiment, the disease to be treated is caused by complement activation. Typically, adenovirus particles are delivered at a dose ranging from 1 particle to 1014 particles per kilogram subject weight, generally between 106 or 108 particles to 1012 particles per kilogram subject weight.

The nucleic acid molecules can be introduced into artificial chromosomes and other non-viral vectors. Artificial chromosomes, such as *ACES* (see, Lindenbaum et al. *Nucleic Acids Res.* 2004 Dec 7;32(21):e172) can be engineered to encode and express the protease or modified protease. Briefly, mammalian artificial chromosomes (MACs) provide a means to introduce large payloads of genetic information into the cell in an autonomously replicating, non-integrating format. Unique among MACs, the mammalian satellite DNA-based Artificial Chromosome Expression System (*ACES*) can be reproducibly generated *de novo* in cell lines of different species and readily purified from the host cells' chromosomes. Purified mammalian ACEs can then be re-introduced into a variety of recipient cell lines where they have been stably maintained for extended periods in the absence of

selective pressure using an ACE System. Using this approach, specific loading of one or two gene targets has been achieved in LMTK(-) and CHO cells.

Another method for introducing nucleic acids encoding the modified protease polypeptides is a two-step gene replacement technique in yeast, starting with a complete adenovirus genome (Ad2; Ketner et al. (1994) *Proc. Natl. Acad. Sci. USA* 91: 6186-6190) cloned in a Yeast Artificial Chromosome (YAC) and a plasmid containing adenovirus sequences to target a specific region in the YAC clone, an expression cassette for the gene of interest and a positive and negative selectable marker. YACs are of particular interest because they permit incorporation of larger genes. This approach can be used for construction of adenovirus-based vectors bearing nucleic acids encoding any of the described modified protease polypeptides for gene transfer to mammalian cells or whole animals.

The nucleic acids can be encapsulated in a vehicle, such as a liposome, or introduced into a cells, such as a bacterial cell, particularly an attenuated bacterium or introduced into a viral vector. For example, when liposomes are employed, proteins that bind to a cell surface membrane protein associated with endocytosis can be used for targeting and/or to facilitate uptake, *e.g.*, capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, and proteins that target intracellular localization and enhance intracellular half-life.

In some situations it is desirable to provide a nucleic acid source with an agent that targets cells, such as an antibody specific for a cell surface membrane protein or a target cell, or a ligand for a receptor on a target cell. Polynucleotides and expression vectors provided herein can be made by any suitable method. Further provided are nucleic acid vectors containing nucleic acid molecules as described above. Further provided are nucleic acid vectors containing nucleic acid molecules as described above and cells containing these vectors.

For *ex vivo* and *in vivo* methods, nucleic acid molecules encoding the protease polypeptide are introduced into cells that are from a suitable donor or the subject to be treated. Cells into which a nucleic acid can be introduced for purposes of therapy include, for example, any desired, available cell type appropriate for the disease or

condition to be treated including, but not limited to, epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, *e.g.*, such as stem cells obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, and other sources thereof.

For *ex vivo* treatment, cells from a donor compatible with the subject to be treated or cells from a subject to be treated are removed, the nucleic acid is introduced into these isolated cells and the modified cells are administered to the subject. Treatment includes direct administration, such as, for example, encapsulated within porous membranes, which are implanted into the patient (see, *e.g.*, U.S. Pat. Nos. 4,892,538 and 5,283,187). Techniques suitable for the transfer of nucleic acid into mammalian cells *in vitro* include the use of liposomes and cationic lipids (*e.g.*, DOTMA, DOPE and DC-Chol) electroporation, microinjection, cell fusion, DEAE-dextran, and calcium phosphate precipitation methods. Methods of DNA delivery can be used to express protease polypeptides *in vivo*. Such methods include liposome delivery of nucleic acids and naked DNA delivery, including local and systemic delivery such as using electroporation, ultrasound and calcium-phosphate delivery. Other techniques include microinjection, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer and spheroplast fusion.

In vivo expression of a protease polypeptide can be linked to expression of additional molecules. For example, expression of a protease polypeptide can be linked with expression of a cytotoxic product such as in an engineered virus or expressed in a cytotoxic virus. Such viruses can be targeted to a particular cell type that is a target for a therapeutic effect. The expressed protease polypeptide can be used to enhance the cytotoxicity of the virus.

In vivo expression of a protease polypeptide can include operatively linking a protease polypeptide encoding nucleic acid molecule to specific regulatory sequences such as a cell-specific or tissue-specific promoter. Protease polypeptides also can be expressed from vectors that specifically infect and/or replicate in target cell types

and/or tissues. Inducible promoters can be use to selectively regulate protease polypeptide expression.

Nucleic acid molecules, as naked nucleic acids or in vectors, artificial chromosomes, liposomes and other vehicles can be administered to the subject by systemic administration, topical, local and other routes of administration. When systemic and *in vivo*, the nucleic acid molecule or vehicle containing the nucleic acid molecule can be targeted to a cell.

Administration also can be direct, such as by administration of a vector or cells that typically targets a cell or tissue. For example, tumor cells and proliferating can be targeted cells for *in vivo* expression of protease polypeptides. Cells used for *in vivo* expression of a protease polypeptide also include cells autologous to the patient. Such cells can be removed from a patient, nucleic acids for expression of a protease polypeptide introduced, and then administered to a patient such as by injection or engraftment.

H. Therapeutic Uses

Therapeutic proteases have many potential advantages over traditional therapeutic approaches. Chief among them is the ability to inactivate disease targets in a catalytic manner (*i.e.* a one to many stoichiometry). Additional differentiating advantages include (1) irreversible inactivation; (2) low dosing; (3) small molecular size; (4) the ability to target post-translational modifications; (5) the ability to neutralize high target concentrations; and (6) the ability to target *away* from the active site. As a therapeutic, a protease must still exhibit the following characteristics: (1) access to the molecular target (extracellular), and (2) possess sufficiently stringent specificity for a target critical to a disease state. The protease polypeptides provided herein can be used in the treatment of diseases.

The protease polypeptides and nucleic acid molecules provided herein can be used for treatment of any condition for which activation of the complement pathway is implicated, particularly inflammatory conditions including acute inflammatory conditions, such as septic shock, and chronic inflammatory conditions, such as Rheumatoid Arthritis (RA). Acute and inflammatory conditions can be manifested as an immune-mediated disease such as for example autoimmune disease or tissue injury

caused by immune-complex-mediated inflammation. A complement-mediated inflammatory condition also can be manifested as a neurodegenerative or cardiovascular disease that have inflammatory components. This section provides exemplary uses of, and administration methods for, proteases. These described therapies are exemplary and do not limit the applications of proteases. Such methods include, but are not limited to, methods of treatment of physiological and medical conditions described and listed below. Such methods include, but are not limited to, methods of treatment of sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), lupus erythematosus, Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, respiratory distress syndrome, immune complex (IC)-mediated acute inflammatory tissue injury, multi-organ failure, Alzheimer's Disease (AD), Ischemia-reperfusion injuries caused by events or treatments such as myocardial infarct (MI), stroke, cardiopulmonary bypass (CPB) or coronary artery bypass graft, angioplasty, or hemodialysis, or Guillan Barre syndrome.

Treatment of diseases and conditions with proteases can be effected by any suitable route of administration using suitable formulations as described herein including, but not limited to, subcutaneous injection, oral and transdermal administration. If necessary, a particular dosage and duration and treatment protocol can be empirically determined or extrapolated. For example, exemplary doses of recombinant and native protease polypeptides can be used as a starting point to determine appropriate dosages. Modified proteases that have more specificity and/or selectivity compared to a wildtype or scaffold protease can be effective at reduced dosage amounts and or frequencies. Dosage levels can be determined based on a variety of factors, such as body weight of the individual, general health, age, the activity of the specific compound employed, sex, diet, time of administration, rate of excretion, drug combination, the severity and course of the disease, and the patient's disposition to the disease and the judgment of the treating physician. The amount of active ingredient that can be combined with the carrier materials to produce a single dosage form with vary depending upon the host treated and the particular mode of administration.

Upon improvement of a patient's condition, a maintenance dose of a compound or compositions can be administered, if necessary; and the dosage, the dosage form, or frequency of administration, or a combination thereof can be modified. In some cases, a subject can require intermittent treatment on a long-term basis upon any recurrence of disease symptoms.

1. Immune-mediated Inflammatory Diseases

Proteases and modified proteases described herein, including but not limited to modified MT-SP1 proteases, can be used to treat inflammatory diseases. Inflammatory diseases that can be treated with proteases include acute and chronic inflammatory diseases. Exemplary inflammatory diseases include central nervous system diseases (CNS), autoimmune diseases, airway hyper-responsiveness conditions such as in asthma, rheumatoid arthritis, inflammatory bowel disease, and immune complex (IC)-mediated acute inflammatory tissue injury.

Experimental autoimmune encephalomyelitis (EAE) can serve as a model for multiple sclerosis (MS) (Piddlesden *et al.*, (1994) *J Immunol* 152:5477). EAE can be induced in a number of genetically susceptible species by immunization with myelin and myelin components such as myelin basic protein, proteolipid protein and myelin oligodendrocyte glycoprotein (MOG). For example, MOG-induced EAE recapitulates essential features of human MS including the chronic, relapsing clinical disease course the pathohistological triad of inflammation, reactive gliosis, and the formation of large confluent demyelinated plaques. Proteases and modified proteases can be assessed in EAE animal models. Proteases are administered, such as by daily intraperitoneal injection, and the course and progression of symptoms is monitored compared to control animals. The levels of inflammatory complement components that can exacerbate the disease also can be measured by assaying serum complement activity in a hemolytic assay and by assaying for the deposition of complement components, such as for example C1, C3 and C9.

Complement activation modulates inflammation in diseases such as rheumatoid arthritis (RA) (Wang *et al.*, (1995) *PNAS* 92:8955). Proteases and modified proteases, including modified MT-SP1 polypeptides, can be used to treat RA. For example, proteases can be injected locally or systemically. Proteases can be

dosed daily or weekly. PEGylated proteases can be used to reduce immunogenicity. In one example, type II collagen-induced arthritis (CIA) can be induced in mice as a model of autoimmune inflammatory joint disease that is histologically similar to RA characterized by inflammatory synovitis, pannus formation, and erosion of cartilage and bone. To induce CIA, bovine type II collagen (B-CII) in the presence of complete Freund's adjuvant can be injected intradermally at the base of the tail. After 21 days, mice can be reimmunized using the identical protocol. To examine the effects of a protease or modified protease, including MT-SP1 polypeptides, 3 weeks following the initial challenge with B-CII, a protease or control can be administered intraperitoneally twice weekly for 3 weeks. Mice can be sacrificed 7 weeks following the initial immunization for histologic analysis. To assess the therapeutic affect of a protease on established disease, a protease can be administered daily for a total of 10 days following the onset of clinical arthritis in one or more limbs. The degree of swelling in the initially affected joints can be monitored by measuring paw thickness using calipers. In both models, serum can be drawn from mice for hemolytic assays and measurement of complement markers of activation such as for example C5a and C5b-9. In another example, primate models are available for RA treatments. Response of tender and swollen joints can be monitored in subjects treated with protease polypeptides and controls to assess protease treatment.

Proteases or modified proteases, including but not limited to MT-SP1 polypeptides, can be used to treat immune complex (IC)-mediated acute inflammatory tissue injury. IC-mediated injury is caused by a local inflammatory response against IC deposition in a tissue. The ensuing inflammatory response is characterized by edema, neutrophila, hemorrhage, and finally tissue necrosis. IC-mediated tissue injury can be studied in an *in vivo* Arthus (RPA) reaction. Briefly, in the RPA reaction, an excess of antibody (such as for example rabbit IgG anti-chicken egg albumin) is injected into the skin of animals, such as for example rats or guinea pigs, that have previously been infused intravenously with the corresponding antigen (*i.e.* chicken egg albumin) (Szalai *et al.*, (2000) *J Immunol* 164:463). Immediately before the initiation on an RPA reaction, a protease, or a bolus control, can be administered at the same time as the corresponding antigen by an intravenous injection via the right

femoral vein. Alternatively, a protease can be administered during the initial hour of the RPA reaction, beginning immediately after injection of the antigen and just before dermal injection of the antibody. The effects of a protease on the generation of complement-dependent IC-mediated tissue injury can be assessed at various times after initiation of RPA by collecting blood to determine the serum hemolytic activity, and by harvesting the infected area of the skin for quantitation of lesion size.

Therapeutic proteases, such as those described herein including MT-SP1 polypeptides, can be used to treat sepsis and severe sepsis that can result in lethal shock. A model of complement-mediated lethal shock can be used to test the effects of a protease as a therapeutic agent. In one such example, rats can be primed with a trace amount of lipopolysaccharide (LPS), followed by the administration of a monoclonal antibody against a membrane inhibitor of complement (anti-Crry) (Mizuno M *et al.*, (2002) *Int Arch Allergy Immunol* 127:55). A protease or control can be administered at any time during the course of initiation of lethal shock such as before LPS priming, after LPS priming, or after anti-Crry administration and the rescue of rats from lethal shock can be assessed.

2. Neurodegenerative disease

Complement activation exacerbates the progression of Alzheimer's disease (AD) and contributes to neurite loss in AD brains. Proteases and modified proteases described herein, including but not limited to modified MT-SP1 polypeptides, can be used to treat AD. Mouse models that mimic some of the neuropathological and behavioral features of AD can be used to assess the therapeutic effects of proteases. Examples of transgenic mouse models include introducing the human amyloid precursor protein (APP) or the presenilin 1 (PS1) protein with disease-producing mutations into mice under the control of an aggressive promoter. These mice develop characteristics of AD including increases in beta-amyloid plaques and dystrophic neurites. Double transgenic mice for APP and PS1 mutant proteins develop larger numbers of fibrillar beta-amyloid plaques and show activated glia and complement factors associated with the plaque. Proteases can be administered, such as by daily intraperitoneal or intravenous injections, and the course and progression of symptoms is monitored compared to control animals.

3. Cardiovascular disease

Proteases and modified proteases described herein, including but not limited to modified MT-SP1 proteases, can be used to treat cardiovascular disease. Proteases can be used in the treatment of cardiovascular diseases including ischemia reperfusion injury resulting from stroke, myocardial infarction, cardiopulmonary bypass, coronary artery bypass graft, angioplasty, or hemodialysis. Proteases also can be used in the treatment of the inflammatory response associated with cardiopulmonary bypass that can contribute to tissue injury. Generally, a protease can be administered prior to, concomitantly with, or subsequent to a treatment or event that induces a complement-mediated ischemia reperfusion injury. In one example, a protease can be administered to a subject prior to the treatment of a subject by a complement-mediated, ischemic-injury inducing event, such as for example coronary artery bypass graft of angioplasty.

Effects of a protease on treatment of ischemia reperfusion injury can be assessed in animal models of the injury. In one such model, myocardial ischemia is induced in rabbits that have had an incision made in their anterior pericardium by placing a 3-0 silk suture around the left anterior descending (LAD) coronary artery 5-8 mm from its origin and tightening the ligature so that the vessel becomes completely occluded (Buerke *et al.*, (2001) *J Immunol* 167:5375). A protease, such as for example a modified MT-SP1 polypeptide, or a control vehicle such as saline, can be given intravenously in increasing doses as a bolus 55 minutes after the coronary occlusion (*i.e.* 5 minutes before reperfusion). Five minutes later (*i.e.* after a total of 60 minutes of ischemia) the LAD ligature can be untied and the ischemic myocardium can be reperfused for 3 hours. At the end of the reperfusion period, the ligature around the LAD is tightened. Effects of a protease on ischemia injury can be analyzed by assessing effects on myocardial necrosis, plasma creatine kinase levels, and markers of neutrophil activation such as for example myeloperoxidase activity and superoxide radical release.

In another model of complement-mediated myocardial injury sustained upon perfusion of isolated mouse hearts with Krebs-Henseleit buffer containing 6% human plasma, treatment with proteases or modified proteases can be used to limit tissue

damage to the heart. In such an example, the buffer used to perfuse the hearts can be supplemented with varying doses of proteases, such as but not limited to modified proteases including MT-SP1 polypeptides. The perfused hearts can be assayed for deposition of human C3 and C5b-9, coronary artery perfusion pressure, end-diastolic pressure, and heart rate.

Proteases and modified proteases, such as for example MT-SP1 polypeptides, can be used as therapeutics prior to or following Cardiopulmonary Bypass (CPB) or coronary artery bypass graft to inhibit the inflammatory immune response that often follows bypass and that can contribute to tissue injury. An *in vitro* recirculation of whole blood in an extracorporeal bypass circuit can be used to stimulate platelet and leukocyte changes and complement activation induced by CPB (Rinder *et al.* (1995) *J. Clin. Invest.* 96:1564). In such a model, addition of a protease or modified protease or control buffer, in varying doses, can be added to a transfer pack already containing blood from a healthy donor and porcine heparin, just prior to addition of the blood to the extracorporeal circuit. Blood samples can be drawn at 5, 15, 30, 45, 60, 75, and 90 minutes after recirculation and assayed for complement studies such as for example hemolytic assays and/or complement activation assays to measure for C5a, C3a, and/or sC5b-9. A pretreatment sample of blood drawn before its addition to the extracorporeal circuit can be used as a control. Flow cytometry of blood samples can be performed to determine levels of adhesion molecules on populations of circulating leukocytes (*i.e.* neutrophils) in the blood such as for example CD11b and P-selectin levels.

I. COMBINATION THERAPIES

Wildtype and modified proteases can be used in combination with each other and with other existing drugs and therapeutic agents to treat diseases and conditions. For example, as described herein a number of proteases can be used to treat acute and chronic inflammatory conditions and diseases. Such treatments can be performed in conjunction with other anti-inflammatory drugs and/or therapeutic agents. Examples of anti-inflammatory drugs and agents useful for combination therapies include non steroidal anti-inflammatory drugs (NSAIDs) including salicylates, such as aspirin, traditional NSAIDs such as ibuprofen, naproxen, ketroprofen, nabumetone,

piroxicam, diclofenac, or indomethacin, and Cox-2 selective inhibitors such as celecoxib (Celebrex®) or Rotecoxin (Vioxx®). Other compounds useful in combination therapies include antimetabolites such as methotrexate and leflunomide, corticosteroids or other steroids such as cortisone, dexamethasone, or prednisone, analgesics such as acetaminophen, aminosalicylates such as mesalamine, and cytotoxic agents such as azathioprine (Imuran®), cyclophosphamide (Cytoxan®), and cyclosporine A. Additional agents that can be used in combination therapies include biological response modifiers. Biological response modifiers can include pro-inflammatory cytokine inhibitors including inhibitors of TNF-alpha such as etanercept (Enbrel®), infliximab (Remicade®), or adalimumad (Humira®), and inhibitors of IL-1 such as anakinra (Kineret®). Biological response modifiers also can include anti-inflammatory cytokines such as IL-10, B cell targeting agents such as anti-CD20 antibodies (Rituxmab®), compounds targeting T antigens, adhesion molecule blockers, chemokines receptor antagonists, kinase inhibitors such as inhibitors to MAP Kinase, JNK, or NFκB, and PPAR-γ ligands.

Wildtype and modified proteases also can be used in combination with agents that are administered to treat cardiovascular disease and/or administered during procedures to treat cardiovascular disease such as for example those described herein that contribute to inflammatory conditions associated with complement-mediated ischemia-reperfusion injury. For example, proteases provided herein such as scaffold proteases or modified proteases can be administered in combination with anti-coagulants. Examples of exemplary anti-coagulants include, but are not limited to, heparin, warfarin, acenocoumarol, phenindione, EDTA, citrate, oxalate, and direct thrombin inhibitors such as argatroban, lepirudin, bivalirudin, ximelagatran.

Additional agents, such as other complement inhibitors, can be used as anti-inflammatory drugs in combination therapy with proteases and modified proteases as described herein. Examples of such other complement inhibitors include cobra venom factor (CVF), polyanionic molecules such as heparin, dextran sulphate, polyvinyl sulphate, polylysine, or suramin, natural molecules such as K-76COOH, Rosmarinic acid, or extract of the Chinese medicinal herb Ephedra, synthetic molecules such as afamastat mesilate (FUT-175), a synthetic inhibitor of C1s (C1s-

INH-248), or an inhibitor against C1s and fD (BCX-1470), peptide inhibitors such as compstatin, antibody inhibitors of complement such as anti-C5 (N19-8), a humanized anti-C5 (h5G1.1), anti-C6, or anti-C8 antibodies, and soluble forms of membrane complement regulators such as soluble CR1 (sCR1), soluble DAF (sDAF), soluble MCP (sMCF), or soluble CD59 (sCD59) (Morgan *et al.*, (2003) *Mol Immunol.* 40:159).

Pharmaceutical compositions containing a protease or modified protease described herein can be used to treat any one or more inflammatory diseases or conditions mediated by complement activation. Also provided are combinations of a protease or modified protease and another treatment or compound for treatment of an inflammatory disease or condition. The protease or modified protease and the anti-inflammatory agent can be packaged as separate compositions for administration together or sequentially or intermittently. Alternatively, they can provided as a single composition for administration or as two compositions for administration as a single composition. The combinations can be packaged as kits, optionally with additional reagents, instructions for use, vials and other containers, syringes and other items for use of the modified protease.

J. EXAMPLES

The following examples are included for illustrative purposes only and are not intended to limit the scope of the embodiments provided herein.

Example 1

Cloning and Mutagenesis of MT-SP1

Wildtype MT-SP1 was cloned into the pQE32 bacterial expression vector (Qiagen, SEQ ID NO:345) C-terminal to the 6 histidine tag using the BamH1 and HindIII restriction sites. The construct included pro-region, activation sequence, and protease domain, and contains residues 598 to the C-terminus of the sequence published by Takeuchi *et al.* (1999) *PNAS* 96:11054 and SEQ ID NO:2 (*i.e.* corresponding to residues 598 to 855 of the sequence of amino acids set forth in SEQ ID NO:2). Mutants were generated by the Quikchange site directed mutagenesis (Stratagene). Briefly, a PCR sample reaction was set up containing the wildtype MT-SP1 as a template and oligonucleotide primers designed to contain the desired

mutation (see Table 21). The PCR reaction was as follows in a 50 µl total reaction volume: 5 µl 10X Reaction Buffer, 1 µl MT-SP1 DNA template (100 ng/µl), 0.5 µl 50 µM forward Primer, 0.5 µl 50 µM reverse Primer, 1.0 µl dNTPs, 41.0 µl H_20, and 1.0 µl Pfu Ultra (2.5 units/µl). A control reaction also was performed in the absence of forward or reverse Primers. The PCR reaction conditions were as follows: 95°C for 30 sec, followed by 18 cycles at 95°C for 30 s, 55°C for 60 s, and 72°C for 8 min, 24 s. The reaction was terminated with an elongation step at 72°C for 10 min followed by incubation at 4°C. Each reaction product was digested with DpnI for 1- 2 hours at 37°C. 1.0 ml of the products were transformed into XL-1 Blue Supercompetent cells and plated at 2.0 µl and 20.0 µl on selective agar containing 50 µg/ml carbenicillin.

Table 21: Mutagenesis Primers

Primer	Sequence	SEQ ID NO
F97Dforward	5'-CACCCCTTCTTCAATGAC**GA**CACCTTCGACTATGACATCG-3'	346
F97Dreverse	5'-CGATGTCATAGTCGAAGGTG**TC**GTCATTGAAGAAGGGGTG-3'	347
F97Eforward	5'-CCACCCCTTCTTCAATGAC**GAG**ACCTTCGACTATGACATCGC-3'	348
F97Ereverse	5'-GCGATGTCATAGTCGAAGGT**CTC**GTCATTGAAGAAGGGGTGG-3'	349
F97Aforward	5'-CACCCCTTCTTCAATGAC**GCC**ACCTTCGACTATGACATC-3'	350
F97Areverse	5'-GATGTCATAGTCGAAGGT**GGC**GTCATTGAAGAAGGGGTG-3'	351
F97Wforward	5'-CACCCCTTCTTCAATGAC**TGG**ACCTTCGACTATGACATC-3'	352
F97Wreverse	5'-GATGTCATAGTCGAAGGT**CCA**GTCATTGAAGAAGGGGTG-3'	353
Y146Nforward	5'-GGACACACCCAG**AAC**GGAGGCACTGGC-3'	354
Y146Nreverse	5'-GCCAGTGCCTCC**GTT**CTGGGTGTGTCC-3'	355
Y146Dforward	5'-GGACACACCCAG**GAC**GGAGGCACTGGC-3'	356
Y146Dreverse	5'-GCCAGTGCCTCC**GTC**CTGGGTGTGTCC-3'	357
Y146Eforward	5'-GGGACACACCCAG**GAG**GGAGGCACTGGCG-3'	358
Y146Ereverse	5'-CGCCAGTGCCTCCC**TC**CTGGGTGTGTCCC-3'	359
Y146Aforward	5'-GGGACACACCCAG**GCC**GGAGGCACTGGCG-3'	360
Y146Areverse	5'-CGCCAGTGCCTCC**GGC**CTGGGTGTGTCCC-3'	361
Y146Wforward	5'-GGGACACACCCAGT**GGG**GAGGCACTGGCG-3'	362
Y146Wreverse	5'-CGCCAGTGCCTCCC**CA**CTGGGTGTGTCCC-3'	363
Y146Rforward	5'-GGGGACACACCCAG**AGG**GGAGGCACTGGCGC-3'	364
Y146Rreverse	5'-GCGCCAGTGCCTCCC**CT**CTGGGTGTGTCCCC-3'	365
Q192Rforward	5'-TGGACTCCTGC**CGG**GGTGATTCCGG-3'	366
Q192Rreverse	5'-CCGGAATCAC**CCC**GGCAGGAGTCCA-3'	367
K224Aforward	5'-CGCTCAGAGGAAC**GC**GCCAGGCGTGTACA-3'	368
K224Areverse	5'-TGTACACGCCTGG**CGC**GTTCCTCTGAGCG-3'	369
K224Fforward	5'-GCTGCGCTCAGAGGAAC**TTC**CCAGGCGTGTACACAAG-3'	370
K224Freverse	5'-CTTGTGTACACGCCTGG**GA**AGTTCCTCTGAGCGCAGC-3'	371

The sequences of each of the cloned protease domain MT-SP1 mutants designated by CB numbering is set forth in any of SEQ ID NOS: 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 552-605, or 672-680.

Example 2

Expression and Purification of MT-SP1

Wild-type and modified MT-SP1 were cloned into the pQE32 bacterial expression vector (Qiagen, SEQ ID NO:345) containing an N-terminal 6 histidine tag, prodomain, and protease domain as discussed in Example 1 above and the resulting constructs transformed into BL-21 *E. coli* cells. Cells were grown in 100 mL cultures to an OD of 0.6, and expression of the protease in inclusion bodies was induced by adding IPTG to a final concentration of 1 mM. After 4-6 hours, the bacteria were pelleted by centrifugation and the pellet resuspended in 50 mM Tris pH 8, 500 mM KCl, and 10% glycerol (buffer A). Cells were lysed by sonication and pelleted by centrifugation at 6000x g. Pellets were resuspended in 50 mM Tris pH 8, 6 M urea, 100 mM NaCl and 1% 2-mercaptoethanol (buffer B). Membrane and organelles were pelleted by centrifugation at 10,000x g and the supernatant was passed over a nickel NTA column (Qiagen). The column was washed with 50 mM Tris pH8, 6 M urea, 100 mM NaCl, 20 mM imidazole, 1% 2-mercaptoethanoland 0.01% Tween 20 (buffer D). The column was washed again with buffer D without Tween 20. The protease was then eluted from the column with 50 mM Tris pH 8, 6 M urea, 100 mM NaCl, 1 % 2-mercaptoethanol and 250 mM imidazole (buffer E). The protease was then concentrated to a volume of ~1 mL and then dialyzed at 4°C overnight in 1 L of 50 mM Tris pH8, 3 M urea, 100 mM NaCl, 1% 2-mercaptoethanol, and 10% glycerol. Finally, the protease was dialyzed into 50 mM Tris pH 8, 100 mM NaCl, and 10% glycerol at 4°C overnight. During the last dialysis step, the protease becomes autoactivated by self-cleavage at the juncture between the prodomain and the protease domain at the sequence RQAR/VVGG, resulting in the removal of the 6 histidine tag and prodomain.

Example 3

Expression and Purification of Modified MT-SP1 CB155 in shake flasks

CB155 and related recombinant human serine protease mutants as well as the wild-type MT-SP1 protease were cloned and expressed in *E.coli* as inclusion bodies

as described in Examples 1 and 2 above. The production of the MT-SP1 or mutants was adapted for laboratory scale by pooling up to 30 X 1 L shake flasks for subsequent isolation of the inclusion body pellets for solubilization and refolding. Briefly, the MT-SP1 mutant CB155 plasmid construct was transformed into XL-1 Blue Supercompetent cells and a single fresh colony was picked and grown in 25 ml of luria broth (LB; Difco LB Broth Lennox, approximate formulation per liter: 10.0 g Tryptone, 10.0 g Yeast Extract, 5.0 g Sodium Chloride) containing 50 µg/ml carbenecillin at 37° C overnight. Ten milliliters of the overnight culture was diluted into 1 L of LB in an Ultra Yield Flask (2.5L) and was shaken at 37° C to an OD600 of about 0.6 to about 0.7 (*i.e.* shaken at 37° C for about 2 hours). IPTG (Dioxane Free; Calbiochem) at 1.0 M was added to the culture at a final concentration of 1 mM to induce expression of the protease in inclusion bodies and the culture was shaken for an additional 4 hours at 37° C. The culture was harvested by centrifugation at 6000 rpm in a Sorvall rotor # SLC4000 for 20 minutes.

The cell pellet from the 1 L culture was resuspended in 50 ml of Wash Buffer II (300 mM Sodium Chloride, 50 mM Potassium Phosphate pH 7.4) and was transferred to a rosette cell for sonication. Cells were lysed by sonication as follows: 20 – 50 ml solution for 2 minutes, 30% duty cycle, output = 5-6, on ice, repeated three times; 100+ ml solution for 2 minutes, 60% duty cycle, output = 8, on ice, repeated six times. The sonicated lysate was centrifuged at 7000 rpm for 20 minutes at 4° C. Supernatant was discarded and the pellets were resuspended in 40 ml Wash Buffer I (300 mM Sodium Chloride, 50 mM Potassium Phosphate pH 7.4, 0.5% LDAO) per about 2.0 gram of inclusion bodies using a spatula and vortexing. The inclusion bodies were centrifuged at 9000 rpm for 15 minutes at 4° C, and washed a total of three times in Wash Buffer I. The centrifugation and washing steps were repeated two additional times in Wash Buffer II. The washed inclusion bodies were suspended in 20 ml of denaturing buffer (6 M Guanidine Hydrochloride, 100 mM Tris HCL pH 8.0, 20 mM Dithiothreitol) per about 2.0 grams of inclusion bodies using a spatula to break up the pellet and rocked at room temperature for 30 minutes until the pellet was dissolved or mostly dissolved. Any insoluble material was removed by centrifugation at 9000 rpm in a Sorvall SLA600TC rotor followed by resuspension in 20 ml buffer.

The sample was slowly dripped into a beaker containing 100X volume of refolding buffer (100 mM Tris HCL pH 8.0, 150 mM NaCl, 5 mM reduced Glutathione, 0.05M oxidized glutathione, 1.5 M L-Arginine mono hydrochloride) and stirred slowly at 4° C for 72 hours. The sample was diluted to 1 M final concentration of Arginine-HCL in 50 mM Tris pH 8.0/ 50 mM NaCl and then concentrated to about 700 ml using cross-flow filtration. The sample was then transferred to the VivaFlow (Sartorius, Edgewood NY) and further concentrated to a final volume of about 300 ml. The sample was dialyzed into 50 mM Tris pH 8.0/50 mM NaCl (8L) overnight. Some precipitation of the sample occurred. The sample was centrifuged at 9000 rpm to remove the precipitation.

The sample was incubated at room temperature until auto-activation of the protease occurred by cleavage of the proregion to release the mature enzyme. The autoactivation occurs during the purification process. Activity was monitored by SDS-PAGE (a 3 kilodalton shift). Activity also was monitored by enzyme activity as assessed by cleavage of a fluorogenic substrate. To measure enzyme activity, protease was diluted from 1:20 fold to 1:100 fold in assay buffer containing 50 mM Tris pH 8.0, 50 mM NaCl and 0.01% Tween-20. Five µl of the diluted protease was mixed with 50 µl of 100 µM Ac-RQAR-AMC substrate, and the fluorescence was measured in a fluorescence spectrophotometer (Molecular Devices Gemini XPS) at an excitation wavelength of 380 nm, an emission wavelength of 450 nm and using a cut-off filter set at 435 nm. Activity was assessed over time as the sample was allowed to incubate at room temperature for about 24 to 72 hours until the activity stabilized. For more dilute samples, more time may be needed. Typically, the protease was allowed to achieve >75% activation before purification by anion exchange.

Once activity stabilized, the sample was dialyzed into 50 mM Hepes pH 6.5 (8 L) overnight. The sample was filtered and loaded onto a SourceQ column. After loading onto the SourceQ column, the sample was washed with 3 column volumes of buffer A (50 mM Hepes pH 6.5) and eluted with a gradient from 0-20% buffer B (50 mM Hepes pH 6.5/ 1 M NaCl) over 10 column volumes. The activity of each fraction was measured, and active fractions were combined and dialyzed into PBS overnight.

The protein sample was concentrated to about 5 ml and benzamidine was added to a final concentration of 20 mM to inhibit the autolysis of CB155. The overall yield of CB155 is typically about 15 to 20 mg CB155/ 1 L cell culture. A yield of 22 mg/liter cell culture has been achieved by production of CB155 at the shake flask scale. The overall yield from inclusion body to native protein was typically less than 10%. Titers in the fermentation up to 3g/L have been achieved in shake flasks.

The purified protein was assayed for specific activity, purity, and endotoxin levels. The specific activity or amount of active protease in each prep was determined by active site titration by incubation with an inhibitor that binds in the active site of the functional protease at varying concentrations followed by addition to a fluorogenic substrate for measurement of substrate proteolysis. The amount of active enzyme was calculated from a plot of the residual protease activity against the inhibitor concentration where the intercept corresponds to the concentration of active protease. Briefly, the purified protein was titrated with ecotin M84R using the method of Harris *et al.* (JBC, 1988, 273:27354-73) by titrating a stock of trypsin with 4-methylumbelliferyl p-guandinobenzoate (MUGB), then a stock of M84R ecotin was titrated with the trypsin. Finally, the purified protease was titrated with the M84R ecotin stock. In each case, the protease was incubated for 30 minutes at 30°C with concentrations of the inhibitor between 0.1 and 2 times the expected protease concentration. Residual activities between 30% and 90% of the uninhibited protease activity were used to plot the data. Enzyme activity was monitored at 30°C in the presence of 40 μM Ac-RQAR-AMC in assay buffer containing 50 mM Tris pH 8.0, 50 mM NaCl, and 0.01% Tween-20 (for trypsin activity, 10 mM CaCl2 was added) on a Gemini XPS spectrafluorimeter (Excitation: 380 nm; Emission: 450 nm; Cut-off: 435 mn). Purity of the protein preparation was assessed by resolution of the protein product on SDS-PAGE followed by staining with Coomassie Blue. The mature protease runs as a single band at 25 kD. The level of endotoxin in each prep was determined by Limulus Amebocyte Lysate Chromo-LAL assay (Associated of Cape Cod) according to the manufacturer's protocol with the following modifications. The protease was diluted 100 fold into LAL Reagent Water (LRW), and split into two tubes. A challenge of 100 endotoxin unit (EU)/mL was added to one tube and LRW to

the other. Then, the sample was diluted 2 fold into stock solutions such that the reaction contained a final concentration of 5 mM tosyl-lysyl-chloromethylketone (TLCK) and 10 mM Tris pH 8.0. Each sample was incubated 2 hours at 37°C to inactivate the protease activity. Samples were further diluted 50 fold and assayed according to the manufacturer's instructions. Results were considered valid if the recovery of the endotoxin challenge was between 50 and 150% of theory. The final purified CB155 typically had > 95% purity by SDS-PAGE, > 90% specific activity, and contained approximately 50 to 500 EU/ml of endotoxin.

Example 4

Large Scale Fermentation of MT-SP1 and mutants

Large scale fermentation of MT-SP1 mutants based on the protocol described in Example 3 has been performed. A 2 liter culture of a selected *E.coli* colony transformed with mutant MT-SP1 was grown overnight in LB media (Difco). The overnight culture was seeded into 50 L fermentation and grown for about 5 hours with shaking at 37° C until absorbance at OD600 reached log phase. Expression of the protease in inclusion bodies was induced with the addition of IPTG to a final concentration of 700 μM and fermentation was continued for an additional 4 hours in fed-batch mode. The culture was harvested by centrifugation to yield a wet weight cell pellet of about 750 grams to 1680 grams. The cell pellet was resuspended and sonicated in 50 mM Tris, pH 8.0, 0.5 M KCl, 10% glycerol, 1 mM beta-mercaptoethanol at 10 ml buffer per 1 gram cell pellet. The sonication conditions were pulse on: 4s, pulse off: 6s, 700W, 30 minutes. The sonicated lysate was centrifuged at 7000 rpm for 30 minutes at 4° C. Supernatant was discarded and the pellets were resuspended in Wash Buffer I (50 mM Tris pH 8.0, 0.5 M KCl, 10% glycerol, 1 mM beta-mercaptoethanol, 0.01% Tween 20) at 10 ml buffer per 1 g of inclusion bodies using a spatula and vortexing. The inclusion bodies were centrifuged and washed two times. The inclusion body yield was about 176 to 506 grams.

Example 5

Production of MT-SP1 in *Pichia pastoris*

The production of multi-milligram amounts of the protease domain of MT-SP1 was carried out by fermentation in a BioFlo 3000 fermentor (New Brunswick Scientific, NJ) equipped with a 3.3 L capacity bioreactor using a SMD1168/

pPIC9K:MTSP1 Sac SCI clone (Friedrich *et al.* (2002) *J. Biol. Chem.*, 277:2160-2168). ZA001 complex media (10g/L yeast extract, 20 g/L peptone, 40 g/L glycerol, 5 g/L ammonium sulfate, 0.2 g/L calcium sulfate dehydrate, 2 g/L Magnesium sulfate hepahydrate, 2 g/L potassium sulfate, 25 g/L sodium hexametaposphate, 4.35 ml/L PTM1) was inoculated with 100 ml of an overnight culture of the *P. pastoris* transformant. The culture was supplemented with 50% glycerol by fed-batch phase and induced for 18-24 hours with methanol controlled at 0.025%.

To purify recombinant MT-SP1 secreted into the culture media, cell and cell debris was removed by centrifugation at 5000g for 30 minutes. The resulting supernatant was decanted, adjusted to pH 8.0 with 10 N NaOH, and filtered through a SartoBran 300 0.45 + 0.2 μM capsule (Sartorius). The supernatant was concentrated to 1 L by ultrafiltration using a 10 kDa ultrafiltration cartridge (NC SRT UF system with AG/Technologies UFP-10-C-5A filter), and the buffer was exchanged by cross-flow filtration into buffer A (50 mM Tris-HCl, 50 mM NaCl, 0.05% tween-80, pH 8.0). The filtration unit was rinsed once with 1 L buffer A, which was combined with the concentrate.

The concentrated MT-SP1-containing solution was applied onto a 150 ml benzamidine column, that had been equilibrated with buffer A, at a flow rate of 8 ml/min. The column was washed with 3 column volumes of buffer B (50 mM Tris-HCl, 1.0 M NaCl, 0.05% tween-80, pH 8.0) and eluted with 3 column volumes of buffer C (50 mM Tris-HCl, 1.0M L-arginine, 0.05% tween-80, pH 8.0). Fractions containing MT-SP1 activity were pooled and concentrated to 10 ml using a JumboSep concentrator (Pall Gelman) and a 10 kDa cutoff membrane. Once concentrated to 10 ml, the buffer was exchanged into buffer D (50 mM Na_2HPO_4, 125 mM NaCl, pH 5.5), and the volume was adjusted to 5- 10 ml. The retentate was removed and the concentrator washed with buffer D, which was added to the concentrate. The total sample volume was adjusted to 15 ml.

The partially purified MT-SP1 from the benzamidine column was passed through a 5 ml Q-sepharose Fast Flow HiTrap Column (Amersham-Pharmacia Biotech) pre-equilibrated with 15 ml of buffer D. The flow through was collected, and the protein concentration was determined by measurement of OD280 (using an

extinction coefficient of 2.012mg/OD280). Purified MT-SP1 was then deglycosylated by the addition of 0.1 µl of Endoglycosidase H (ProZyme, 5 U/ml) per mg of protein and incubation overnight at 4° C with gentle swirling followed by a subsequent anion exchange purification step (not required for CB155 MT-SP1 mutant).

The conductivity of the deglycosylated pool was adjusted to 2.0- 3.0 mS/cm with Nanopure H_2O and the pH was adjusted to 6.5 (about 200 to 300 ml final volume). MT-SP1 was then further purified by anion exchange chromatography by loading directly onto a Pharmacia Akta Explorer system using a 7 ml Source 15Q anion exchange column (Amersham-Pharmacia Biotech). The protein was eluted in a buffer containing 50 mM HEPES, pH 6.5 with a 0-0.33M NaCl gradient over 10 column volumes at a flow rate of 6 ml/min. Fractions containing protein were pooled, and benzamidine was added to a final concentration determined by measurement of OD280 and use of a theoretical extinction coefficient of 2.012mg/OD280.

Example 6

Assessment of Plasma Activity

The activity in plasma of wildtype or modified proteases was determined by cleavage of the peptide substrate Ac-RQAR-AMC, which includes the MT-SP1 auto-activation site. One microliter of a 10 µM protease stock was diluted into 9 µl PBST or 9 µl pooled human citrated plasma (Innovative Research; Sarasota, Florida) (1 µM final). The reaction was incubated for 5 minutes at 37° C. At the end of the incubation, 1 µl of the incubated protease mixture was diluted into 250 µl assay buffer (50 mM Tris, pH 8.0, 50 mM NaCl, 0.01% Tween-20). 1 µl of the Ac-RQAR-AMC substrate (6.25 mM in DMSO) was added to each well of a Nunc black microtiter plate and 50 µl of the diluted, incubated protease mixture was added to the well. Cleavage of the substrate was monitored using a Spectromax fluorescence plate reader by taking kinetic measurements with the excitation wavelength at 380 nm and the emission wavelength at 450 nm. Fractional activity of the protease was calculated as a ratio of the activity of the protease in plasma divided by the activity in PBST.

The plasma activity of wildtype MT-SP1 or a panel of MT-SP1 mutants was determined in parallel with assessment of the proteases in hemolytic assays (see Example 7 below). The results are set forth in Table 23 below.

Example 7

Hemolytic Assays for Screening and Titrating Protease Activity by Detection of Complement-Induced Hemolysis of Red Blood Cells

The functional activity of the complement system can be assessed using traditional hemolytic assays, which screen for function of the total complement pathway by determining the ability of the sample to lyse erythrocytes. Serial dilutions of the sample to be analyzed are incubated with antibody-sensitized sheep erythrocytes at a defined temperature. The number of red cells lysed is determined by spectrophotometric absorbance of released hemoglobin, which has a linear relationship to complement protein levels in the 50% lysis range. The results are usually expressed as reciprocal dilutions of the sample required to produce 50% lysis. Thus, when evaluating the activity of the components of the classical pathway, a CH_{50} value can be determined. Tests evaluating the functional activity of the alternative pathway to determine the AH_{50} (the titer at which 50% hemolysis occurs) use guinea pig, rabbit or chicken erythrocytes as target cells. Activation of the classical pathway is blocked by the addition of EGTA and Mg to the alternative pathway hemolytic assay.

Hemolytic assays can be modified to determine the effect of a given protease on complement activation. Protease is incubated with the plasma prior to co-incubation with the erythrocytes. Cleavage of complement products by the proteases will result in decreased complement activity. By incubating the plasma with serial dilutions of the proteases, an IC_{50} can be determined, which is the concentration of protease at which 50% inhibition of complement activity is achieved.

A. Classical Hemolytic Assays

1. Classical Hemolytic Assay: preincubation with 20% plasma

a. To assess complement activation following treatment with proteases, human plasma with sodium citrate as an anticoagulant (Innovative Research, Inc.) was diluted into PBST to a final concentration of 20% (10 µl plasma in 40 µl PBST)

before addition of wildtype MT-SP1, CB155, or CB42 diluted to a final concentration of 0-1 μM. The reaction was incubated at 37°C for 1 hour. The plasma solution was further diluted to a final concentration of 0.5% in a solution of sheep's red blood cells activated with IgG (6.25 μl plasma solution in 250 μl sheep's red blood cell solution, Diamedix (Miami, FL)). The solution was incubated with shaking at room temperature for 45 minutes. The cells were spun down at 2000 rpm for 2 minutes and 100 μl of the supernatant was removed and placed in a clear 96-well microtiter plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm. The IC_{50} (nM) of hemolysis by wildtype MT-SP1, CB155, and CB42 was 131 nM, 94 nM, and 67 nM, respectively.

A panel of MT-SP1 modified proteases were tested for inhibition of hemolysis. Diluted human plasma containing sodium citrate as an anticoagulant was incubated with 200 nM of wildtype MT-SP1, CB12, CB13, CB31, CB32, CB40, CB41, CB42, CB43, CB44, CB45, CB64, CB66, CB67, and CB155. The reaction was incubated at 37° C for 1 hour. The plasma solution was further diluted to a final concentration of 0.5% in a solution of sheep's red blood cells activated with IgG and hemolysis was assayed as described above. The CH50 value was determined. The fraction of hemolysis was determined by comparing the CH50 value of the wildtype or modified proteases compared to a sample containing no added protease (positive control) where the fraction of hemolysis of the positive control was set at 1.00. Table 22 depicts the raw fraction of hemolysis values. The data shows that all proteases tested inhibited hemolysis by at least 50% compared to the positive control with hemolysis completely inhibited in the presence of CB42.

Table 22: Inhibition of Hemolysis by a Panel of MT-SP1 Variants

Protease	Fraction of Hemolysis
Wildtype	0.14
CB12	0.22
CB13	0.50
CB31	0.51
CB32	0.38
CB40	0.48
CB41	0.32

CB42	0.00
CB43	0.23
CB44	0.48
CB45	0.27
CB64	0.34
CB66	0.44
CB67	0.33
CB155	0.09
Negative control	0.00
Positive control	1.00

b. In another experiment, to assess classical complement activation following treatment with proteases, proteases were initially diluted in PBST to a concentration of 5.0 μM for screening protocols, while serial dilutions of the proteases from 50 μM to 0.390 μM were used for protocols to determine the IC_{50}. MT-SP1 or modified proteases were preincubated with a final concentration of 20% plasma in an 0.2ml tube by combining 2 μl of the diluted protease solution, 10 μl of human plasma (with sodium citrate as an anticoagulant; Innovative Research, Inc.) and 38 μl of PBST. This resulted in a further dilution of the protease to give a final concentration of 200nM protease for the screening protocol, and 2.0 μM to 0.0156 μM protease for the IC_{50} protocol. A no-protease control (10 μl plasma and 40 μl PBST) and a background control (50 μl PBST only) also were included in the assays. The reaction was incubated at 37°C for 1 hour. Sensitized sheep erythrocytes (Diamedix, Miami, FL) were added to polypropylene 96-well plates at a volume of 120 μl per well, and 3μl of the plasma/protease solution was mixed into each well giving a final plasma concentration of 0.5%. The solution was incubated with shaking at room temperature for 45 minutes. The cells were spun down at 2000 rpm for 5 minutes in a Sorvall table top centrifuge to pellet the unbroken cells, and 100 μl of the supernatant was removed and placed in a clear 96-well microtiter plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm. The fraction hemolysis was calculated by subtracting the background control from all of the wells, then dividing the experimental samples by the no-protease control (positive control), where the fraction of hemolysis of the positive control was

set at 1.00. The IC_{50} (nM) of hemolysis by the proteases were measured by plotting the fraction hemolysis versus protease concentration on a 4 parameter logistic curve fit (SoftMax Pro software, Molecular Devices, CA).

A panel of MT-SP1 modified proteases were tested for inhibition of hemolysis through cleavage of one or more components of the classical complement pathway. Diluted human plasma containing sodium citrate as an anticoagulant was incubated with either 200 nM, or serial dilutions from 2.0 μM to 0.0156 μM, of wildtype MT-SP1 (CB200), CB12, CB16, CB17, CB20, CB21, CB42, CB43, CB44, CB45, CB66, CB80, CB82, CB155, CB212, CB213, CB214, CB216, CB218, CB219, CB232, CB235, CB238, CB244, CB245, CB251, CB252, CB255, CB257, CB268, CB274, CB331, CB332, CB349, CB350, CB351, CB353, CB357, CB367, CB373, CB377, CB381, CB383, CB385, CB387, CB388, CB403, CB409, CB412, CB413, CB421, CB422, CB423, CB450, CB451, CB458, CB464, CB486, CB487, CB488, CB489 and CB490. The reaction was incubated at 37° C for 1 hour. The protease/plasma solution was further diluted in sensitized sheep erythrocytes and hemolysis was assayed as described above. The fraction hemolysis and ID_{50} was determined. Table 23 depicts the fraction hemolysis at 200 nM (Classical 200nM hemolysis) and the IC_{50} for each protease (20% plasma pre-incubation).

2. Classical Hemolytic Assay: preincubation with 90% plasma

The modified classical hemolytic assay can be adapted further to measure the inhibitory activity of proteases under more physiological conditions by adjusting the plasma and protease concentrations. Proteases were initially diluted in PBST to a concentration of 50 μM for screening protocols, while serial dilutions of the proteases from 200 μM to 1.56 μM were used for protocols to determine the IC_{50}. MT-SP1 or modified proteases were preincubated with a final concentration of 90% plasma in an 0.2ml tube by combining 2 μl of the diluted protease solution, 18 μl of human plasma (with sodium citrate as an anticoagulant; Innovative Research, Inc.). This resulted in a further dilution of the protease to give a final concentration of 5.0 μM protease for the screening protocol, and 20 μM to 0.156 μM protease for the IC_{50} protocol. A no-protease control (18 μl plasma and 2 μl PBST) and a background control (20 μl PBST only) also were included in the assays. The reaction was

incubated at 37° C for 1 hour. The reaction mixtures were further diluted to 20% plasma with the addition of 70 µl PBST. Sensitized sheep erythrocytes (Diamedix, Miami, FL) were concentrated to 10X by pelleting a 3.0 ml aliquot, removing 2.7 ml of buffer and resuspending the cell pellet in the remaining 0.3 ml buffer. The concentrated sensitized erythrocytes were added to polypropylene 96-well plates at a volume of 12 µl per well. Preincubated protease/plasma mixtures at 6 µl or 60 µl were added to the erythrocytes to give a final concentration of 1% plasma or 10% plasma, respectively, in a final volume of 120 µl (PBST added to final volume). The solution was incubated with shaking at room temperature for 45 minutes. The cells were spun down at 2000 rpm for 5 minutes to pellet the unbroken cells, and 100 µl of the supernatant was removed and placed in a clear 96-well microtiter plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm. The fraction hemolysis was calculated by subtracting the background control from all of the wells, then dividing the experimental samples by the no-protease control (positive control), where the fraction of hemolysis of the positive control was set at 1.00. The IC_{50} (nM) of hemolysis by the proteases were measured by plotting the fraction hemolysis vs protease concentration on a 4 parameter logistic curve fit (SoftMax Pro software, Molecular Devices, CA).

Wildtype MT-SP1 (CB200), and MT-SP1 mutants CB252 and CB377 were tested for inhibition of hemolysis following preincubation with 90% plasma. Preincubated protease/plasma mixtures (at a final concentration of 20 nM to 2000 nM protease) were incubated with sensitized erythrocytes at a final plasma concentration of 10% and hemolysis was assessed as described above. The IC_{50} of hemolysis was determined as described above. The IC_{50} of CB200, CB252 and CB377 was 967 nM, 379 nM, and 205 nM, respectively.

Modified MT-SP1 CB450 also was assessed for *in vitro* classical pathway-induced hemolysis following preincubation with 90% plasma. Preincubated protease/plasma mixtures (at a final concentration of 20 nM to 2000 nM protease) were incubated with sensitized erythrocytes at a final plasma concentration of 1% and 10% and hemolysis was assessed as described above. The results show that CB450 dose-dependently decreased hemolysis induced by 1% or 10% plasma, with slightly

greater inhibition of hemolysis observed upon induction by 1% plasma. For example, there was no detectable hemolysis observed upon induction in 1% plasma in the presence of 100 nM or greater CB450, whereas induction in 10% plasma required a higher yield of protease to achieve complete inhibition of hemolysis (*i.e.* about 750 nM or greater CB450 protease).

B. Alternative Hemolytic Assay

1. Alternative Hemolytic Assay: preincubation with 20% plasma

To assess alternative complement activation following treatment with proteases, proteases were initially diluted in GVB/Mg/EGTA buffer containing gelatin veronal buffer (GVB; Comptech) with 10mM $MgCl_2$ and 8mM EGTA. The proteases were diluted to a concentration of 7.5 μM for screening protocols, while serial dilutions of the proteases from 30 μM to 0.2344 μM were used for protocols to determine the IC_{50}. MT-SP1 or modified proteases were preincubated with a final concentration of 20% plasma in a well of a 96-well polypropylene plate by combining 5 μl of the diluted protease solution, 15 μl of human plasma (with sodium citrate as an anticoagulant; Innovative Research, Inc.) and 55 μl of GVB/Mg/EGTA buffer. This resulted in a further dilution of the protease to give a final concentration of 500nM protease for the screening protocol, and 2.0 μM to 0.0156 μM protease for the IC_{50} protocol. A no-protease control (15 μl plasma and 60 μl GVB/Mg/EGTA) and a background control (75 μl GVB/Mg/EGTA only) also were included in the assays. The reaction was incubated at room temperature for 1 hour. Following the incubation, 5 μl GVB/Mg/EGTA was added to the incubated mixture, followed by 20 μl of washed chicken Alsevers (50% mix of whole blood from chickens and alsevers solution, which contains anti-coagulants; Colorado Serum Company, CO) giving a final plasma concentration of 15%. Prior to the addition, the chicken Alsevers were sensitized as described in Example 19 below and the cells were centrifuged and washed 3 times in cold PBS and resuspended in 10 ml GVB/Mg/EGTA, and stored on ice until use. The plates were shaken at 37°C for 1 hour. The cells were spun down at 2000 rpm for 5 minutes to pellet the unbroken cells, and 100 μl of the supernatant was removed and placed in a clear 96-well microtiter plate. Release of hemoglobin

from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm. The fraction hemolysis was calculated by subtracting the background control from all of the wells, then dividing the experimental samples by the no-protease control (positive control), where the fraction of hemolysis of the positive control was set at 1.00. The IC_{50} (nM) of hemolysis by the proteases were measured by plotting the fraction hemolysis vs protease concentration on a 4 parameter logistic curve fit (SoftMax Pro software, Molecular Devices, CA).

A panel of MT-SP1 modified proteases were tested for inhibition of hemolysis through cleavage of one or more components of the alternative complement pathway. Human plasma containing sodium citrate as an anticoagulant was incubated with either 500 nM, or serial dilutions from 2.0 μM to 0.0156 μM, of wildtype MT-SP1 (CB200), CB12, CB16, CB17, CB20, CB21, CB42, CB43, CB44, CB45, CB66, CB80, CB82, CB155, CB212, CB213, CB214, CB216, CB218, CB219, CB232, CB235, CB238, CB244, CB245, CB251, CB252, CB255, CB257, CB268, CB274, CB331, CB332, CB349, CB350, CB351, CB353, CB0357, CB367, CB373, CB377, CB381, CB383, CB385, CB387, CB388, CB403, CB409, CB412, CB413, CB421, CB422, CB423, CB450, CB451, CB458, CB464, CB486, CB487, CB488, CB489 and CB490. The reaction was incubated at room temperature for 1 hour. The protease/plasma solution was further diluted in chicken erythrocytes and hemolysis was assayed as described above. The fraction hemolysis and ID_{50} was determined. Table 23 depicts the fraction hemolysis at 500 nM (Alternative 500nM hemolysis) and the IC_{50} for each protease (20% plasma pre-incubation).

Table 23: Assessment of Hemolysis and Plasma Activity by a Panel of MT-SP1 mutants

CB#	Mutations	Classical 200nM Hemolysis	Alternative 500 nM Hemolysis	Classical IC_{50} Hemolysis (nM)	Alternative IC_{50} Hemolysis (nM)	Plasma Activity
CB200	**wt**	**0.14**	**0.14**	**131**	**545**	**0.2**
CB12	F97D	0.109	0.229	127.15		0.2
CB16	Y146F	0.058	0.049	182.6	204.95	0.23
CB17	L172N	0.198	0.044	211.7	180	0.19
CB20	Q175D	0.106	0.071	125.4	138.4	0.13
CB21	Q175E	0.156	0.047	123.7	81.7	0.16

CB42	Y146E	0.072	0.088	91.6	117.5	0.19
CB43	Y146A	0.195	0.226	160.2		0.07
CB44	Y146W	0.229	0.114	157.33		0.14
CB45	Y146R	0.195	0.297	170.42		0.07
CB66	K224A	0.236	0.097	166.3	102.2	0.24
CB80	R60cD	0.085	0.463	82	367	0.23
CB82	R60cW	0.147	0.48	74.8	283	0.29
CB155	Y146D/K224F	0.09	0.29	94	221	0.36
CB212	Y146N/K224F	0.477	0.538	371.5		0.47
CB213	Y146E/K224F	0.188	0.21	168.5		0.29
CB214	Y146A/K224F	0.197	0.32	171.25		0.42
CB216	Q192V/K224F	0.892	0.866	1200		0.47
CB0218	Q192F/K224F	0.975	0.947	1000		0.09
CB219	Y146D/Q192A/K224F	0.929	0.887	1100		0.63
CB232	Y146E/K224L	0.024	0.082	74.8	94.2	0.23
CB235	Y146E/K224A	0.035	0.126	96.7	89.8	0.26
CB238	Y146D/K224L	0.023	0.105	91.4	149.3	0.53
CB244	Y146D/K224R	0.046	0.562	66.08	617.5	0.18
CB245	Y146D/K224N	0.05	0.51	127.84	421.5	0.32
CB251	Y146E/K224R	0.052	0.47	57.57	625	0.19
CB252	Y146E/K224N	0.025	0.405	38.98	451.5	0.27
CB255	Y146E/K224T	0.115	0.84	179.46	580.1	0.55
CB257	Y146E/K224Y	0.032	0.548	118.65	158	0.44
CB268	Q221aD	0.049	0.359	55.3	512	0.2
CB274	G147E	0.102	0.441	80.7	311.5	0.23
CB331	I41D/Y146D/K224L	0.8	0.19	325.15	76.4	0.34
CB332	I41E/Y146D/K224L	0.254	0.124	150.05	52.3	0.53
CB349	I41D/Y146D/K224F	0.775	0.188	359.28	110.17	0.61
CB350	I41E/Y146D/K224F	0.729	0.24	284.14	177.07	0.69
CB351	I41T/Y146D/K224F	0.144	0.245	50.31	71.25	0.71
CB353	H143V/Y146D/K224F	0.278	0.193	160.85	461.4	0.26
CB357	I41T/Y146D/K224L	0.068	0.203	88.58	126.26	0.41
CB367	Y146D/Q175D/K224R	0.1	0.219	86	146.92	0.31
CB373	Y146E/Q175D/K224R	0.093	0.268	73.48	123.2	0.34
CB377	Y146E/Q175D/K224N	0.052	0.284	58.7	102.87	0.61
CB381	Y146D/Q175H/K224L	0.169	0.219	111.55	291.86	0.25
CB383	Y146D/Q175L/K224L	0.153	0.137	88.03	266.25	0.14
CB385	Y146D/Q175F/K224L	0.184	0.207	123.13	472.11	0.18
CB387	Y146D/Q175W/K224L	0.147	0.115	91.2	224.69	0.25
CB388	Y146D/Q175Y/K224L	0.272	0.194	114.83	317.21	0.23
CB403	Y146D/D217F/K224L	0.262	0.406	152.37	221.09	0.054
CB409	I41A/Y146D/K224F	0.22	0.174	281.2		0.498
CB412	I41L/Y146D/K224F	0.165	0.247	262.5		0.547

CB413	I41F/Y146D/K224F	0.222	0.215	251.11		0.446
CB421	I41T/Y146D/Q175D/K224F	0.714	0.271	478.9		0.585
CB422	I41T/Y146E/Q175D/K224N	0.05	0.15	50.35		0.511
CB423	I41T/Y146E/K224L	0.061	0.176	180.19		0.221
CB450	I41T/Y146D/G151L/K224F	0.255	0.223	269.14		0.287
CB451	Y146D/Q221aL/K224S	0.147	0.416	130.46	173.07	0.12
CB458	Y146E/Q221aE/K224R	0.136	0.58	93.25	332.95	0.21
CB464	Y146E/Q221aE/K224F	0.02	0.124	52.3	91.15	0.54
CB486	I41T/Y146E/Q175D/K224R	0.014	0.128	43.36		
CB487	I41T/Y146E/G151L/Q175D/K224N	0.026	0.173	52.87		0
CB488	I41T/Y146E/G151L/Q175D/K224F	0.086	0.195	72.61		
CB489	I41T/Y146E/G151L/Q175D/K224L	0.038	0.143	50.56		
CB490	I41T/Y146E/G151L/Q175D/K224R	0.031	0.125	52.63		

2. **Alternative Hemolytic Assay: preincubation with 90% plasma**

The modified alternative hemolytic assay can be adapted further to measure the inhibitory activity of proteases, such as for example those with low activity, by adjusting the plasma and protease concentrations. Proteases were initially diluted in GVB/Mg/EGTA to a concentration of 50 μM for screening protocols, while serial dilutions of the proteases from 200 μM to 1.56 μM were used for protocols to determine the IC_{50}. MT-SP1 or modified proteases were preincubated with a final concentration of 90% plasma in a well of a 96-well polypropylene plate by combining 2 μl of the diluted protease solution with 18 μl of human plasma (with sodium citrate as an anticoagulant; Innovative Research, Inc.). This resulted in a further dilution of the protease to give a final concentration of 5.0μM protease for the screening protocol, and 20 μM to 0.156 μM protease for the IC_{50} protocol. A no-protease control (18 μl plasma and 2 μl GVB/Mg/EGTA) and a background control (20 μl GVB/Mg/EGTA only) also were included in the assays. The reaction was incubated at room temperature for 1 hour. After the incubation, 80 μl of GVB/Mg/EGTA was added to the incubated plasma/protease mix, followed by the addition of 20 μl of washed chicken cells (described above), giving a final plasma concentration of 15%. The plates were shaken at 37°C for 1 hour. The cells were spun down at 2000 rpm for 5 minutes to pellet the unbroken cells, and 100 μl of the supernatant was removed and placed in a clear 96-well microtiter plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm. The

fraction hemolysis was calculated by subtracting the background control from all of the wells, then dividing the experimental samples by the no-protease control where the fraction of hemolysis of the positive control was set at 1.00. The IC_{50} (nM) of hemolysis by the proteases were measured by plotting the fraction hemolysis vs protease concentration on a 4 parameter logistic curve fit (SoftMax Pro software, Molecular Devices, CA).

Modified MT-SP1 CB450 was assessed for *in vitro* alternative pathway-induced hemolysis following preincubation with 90% plasma. Preincubated protease/plasma mixtures (at a final concentration of 20 nM to 2000 nM protease) were incubated with chicken cells at a final plasma concentration of 15% and hemolysis was assessed as described above. The results show that CB450 dose-dependently decreased hemolysis induced by 15% plasma, with no detectable hemolysis of the red blood cells observed at about 500 nM or greater CB450 protease.

Example 8

Detection of Complement-Induced Hemolysis of Red Blood Cells using Complement-Depleted Sera

a. To assess complement activation by purified complement factors treated in the presence or absence of wildtype MT-SP1, CB155, or CB42 protease, purified complement factors C2, C3, C4, and C5 and C2-, C3-, C4- and C5- complement depleted media were purchased from Quidel. Purified complement proteins (C2, C3, C4, or C5) were incubated with 100 nM wildtype MT-SP1, CB155 or CB42 protease at 37° C for 3 hours. The concentration of the purified protein used in the reaction was 5 µM. One microliter of the reaction along with 1 µl of the appropriate complement depleted sera was added to 100 µl of sensitized sheep red blood cells and assayed for hemolytic activity as described in Example 7 above. The CH50 values of hemolysis were determined. The fraction of hemolysis of the samples was determined by comparing the CH50 value of the sample to the C2-sera containing sample containing no added protease which was set at 1.00 Table 24 depicts the raw fraction of hemolysis values. Wildtype MT-SP1, CB155, and CB42 proteases inactivate C2 and C3, but not C4 and C5 as determined by an inhibition of hemolysis.

Table 24: Hemolysis by Protease-incubated Complement Proteins Added Back to

Complement-depleted Sera

Protease	Fraction of Hemolysis
C2	1
C2 + WT	0
C2 + CB155	-0.00104
C2 + CB42	0.071429
C3	1.032325
C3 + WT	0.008342
C3 + CB155	0.07195
C3 + CB42	0.122449
C4	0.957766
C4 + WT	0.970027
C4 + CB155	0.944142
C4 + CB42	1.040816
C5	0.983651
C5 + WT	0.888283
C5 + CB155	0.942779
CB + CB42	1.020408

b. In another experiment, a panel of complement proteins were treated in the presence or absence of MT-SP1 (CB200), CB252, and CB377 to assess consequences on inactivation of purified complement proteins by the proteases. Purified complement proteins (all from Quidel; San Diego, CA) were incubated at their physiological serum concentrations (C1q: 180 μg/ml; C2: 25 μg/ml; C3: 1000 μg/ml; C4: 500 μg/ml; C5: 75 μg/ml; C6: 70 μg/ml; C8: 80 μg/ml; C9: 60 μg/ml) in PBST with 25 nM CB200, CB252, or CB377 protease. One μl of the reaction was added to 100 μl of sensitized sheep red blood cells in the presence of 1 μl of sera that was depleted for the corresponding complement factor (all depleted sera purchased from Quidel). As controls, a no protease control, depleted sera only, and normal sera only were included in the reactions. The samples were incubated in wells of a 96-well plate for 1 hour at room temperature with shaking. The cells were spun down by centrifugation to pellet the unbroken cells, and 85 μl of the supernatant was removed and transferred to a clear 96-well microtiter plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm.

The results showed that the control depleted sera in the absence of the added corresponding purified complement protein showed little to no hemolysis as assessed by the OD415 reading, whereas the control normal sera exhibited hemolysis as assess by an OD415 of about 0.4. For each of the reactions where the corresponding purified complement protein was added back to the depleted sera (no protease control), the OD415 reading was comparable to that observed with the normal sera. Preincubation of the complement proteins C1q, C3, C4, C5, C6, C7, C8, or C9 with CB200, CB252, or CB377 showed no decreased hemolysis as compared to normal sera or the no protease control. In contrast, preincubation of C2 with CB200, CB252, or CB377 resulted in an inhibition of hemolysis as assessed by a reduced OD415 absorbance to levels comparable to the depleted sera control.

Example 9

Visualization of the Proteolytic Cleavage of Complement Component C2 in Human Plasma by Western Blotting

a. To visualize the proteolytic cleavage products, human plasma was diluted to 5% in 40 µl PBST and purified CB155, CB200, or CB42 was added to a final concentration between 0 and 500 nM. The samples were incubated for 1 hour at 37°C. Twenty microliters of the reaction, or purified complement C2 as a control (CompTech), was separated by SDS-PAGE on a 4-12% Tris-Glycine gel at 200 V for 35 minutes using a Novex Mini-Cell Surelock apparatus (Invitrogen), then transferred to PVDF membrane (Invitrogen) using a Bio-Rad Transblot SD semi-dry transfer cell. The membrane was blocked 1 hour with 5% dry milk in TBST (Tris-buffered saline with 1% Tween 20) followed by washing and incubation with 1:3000 dilution of goat anti-human C2 antisera (Quidel) in 5% dry milk/TBST overnight at 4° C. The membrane was washed again three times in TBST for 10 minutes each wash, and incubated with 1:10,000 HRP conjugated rabbit anti-goat antibody (Invitrogen, Carlsbad, CA) in 5% dry milk/TBST for one hour at room temperature. The filter was washed three times in TBST for 10 minutes each wash, and the C2 in the plasma, and its cleavage products, were developed with ECL Plus Western Blotting Detection System (Amersham Biosciences) according to the manufacturer's instructions. Densitometry was performed on a FluorChem imaging system (Alpha Innotech Corp.) using AlphaEase FC Fluorchem 8800 software, version 3.1.2 (Alpha Innotech Corp.).

Densitometry was used to determine the ratio of uncleaved product to cleaved product. The IC_{50} of the proteases for cleavage of C2 was determined to be as follows: CB200: 15.7 nM; CB155: 18.4 nM; and CB42:11.9nM.

b. In another experiment, the cleavage of C2 and C3 by wildtype MT-SP1 (CB200) and mutant MT-SP1 CB252 and CB377 was compared. Nine microliters of human citrated plasma (Innovative Research) was incubated with 1 µl of protease to give a final concentration of protease ranging from 0 to 2000 nM. Incubations were performed for 1 hour at 37 °C. One microliter of the preincubated protease/plasma reaction was combined with 10 µl (for assessment of C2) or 1000 µl (for assessment of C3) NuPAGE LDS same buffer and sample reducing reagent (Invitrogen, Carlsbad, CA) and boiled for 5 minutes. In parallel, 10 µl of the boiled samples were loaded onto 4 - 12% NuPAGE Bis-Tris gradient gels (Invitrogen) and run at 200 V for 35 minutes using the Novex Mini-Cell Surelock apparatus (Invitrogen) for protein separation, followed by transfer to a PVDF membrane filter (Invitrogen) using a Bio-Rad Transblot SD semi-dry transfer cell. The membranes were blocked with 5 % dry milk (Bio-Rad, Hercules, CA) in TBST (Tris-buffered saline with 1% Tween 20) for 1 hour. The membranes were then incubated with goat anti-human C2 (Quidel) or goat anti-human C3 at 1:2000 in 5% dry milk/TBST overnight at 4C. The membranes were washed three times in TBST for 10 minutes, and then incubated with HRP-conjugated anti-goat secondary antibody (Zymed; San Francisco, CA) at 1:2000 in 5% dry mil/TBST for one hour at room temperature. The membranes were washed three times in TBST for 10 minutes, and developed with ECL Plus Western Blotting Detection System (Amersham Biosciences; Piscataway, NJ). Densitometry was performed with a FluorChem imaging system (Alpha Innotech Corp; San Leandro, CA) using Alpha Ease FC Fluorchem 8800 software, version 3.1.2 (Alpha Innotech Corp). The results show that each of CB200, CB252, and CB377 cleaved C2 in human plasma in a dose-dependent manner whereas none of the tested proteases cleaved C3 in human plasma as compared to the no protease control even at the highest concentration of protease (2000 nM). Degradation of C2 was noticeable by Western blot at 500 nM of each of the tested proteases with little to no detectable C2

observed at 1000 nM and complete degradation of C2 evident at 2000 nM of tested proteases.

Example 10

Assessment of Alternative and Classical Hemolysis and Correlation with Proteolytic Cleavage of Complement Component C3 in Human Plasma

A panel of proteases were screened at a final concentration of 200 nM (classical) or 500 nM (alternative) for their effects on classical hemolysis or alternative hemolysis, respectively, following preincubation with human plasma as set forth in Example 7, A.1 and B.1 as described above. The panel of proteases that were tested included wildtype (CB200), CB238, CB331, CB349, CB357, CB367, CB377, and CB387. CB200, CB357, CB367, and CB387 inhibiting both the classical and alternative hemolysis to varying degrees. CB238 and CB377 showed little alternative hemolysis inhibition, but did show substantial inhibition of classical hemolysis. CB331 and CB349 showed little classical hemolysis inhibition, but did exhibit inhibition of alternative hemolysis. The results showed that CB331, CB349, and CB387 were selective for cleaving the alternative pathway as compared to the classical pathway.

The hemolysis results were correlated to cleavage of C3 in plasma as assessed by the visualization of C3 in the presence or absence of protease. Samples from the alternative hemolysis assay also were examined by Western blot for C3 as described in Example 9 above. Consistent with the alternative hemolysis results, the results show that CB331, CB349, and CB387 cleave C3 as assessed by decreased C3 product as compared to the no protease treated plasma sample.

Example 11

Cleavage of Purified Complement Components and Identification of Cleavage Sites

To determine increased specificity of modified proteases for a target protein compared to a scaffold or wildtype protease, purified complement factors C2, iC3, and iC4 were purchased from Quidel Corporation (San Diego, CA). 5 μg of each protein was diluted to a final concentration of 5 μM in PBST. MT-SP1, CB155, or Factor I were added to a final concentration of 100 nM, and the reaction was

incubated at 37°C for 5 hours. N-linked glycosylation was removed by denaturing the protein and treating with PNGaseF according to the manufacturer's protocol (New England BioLabs, Ipswich, MA). The target proteins were separated by SDS-PAGE on a 4-12% Tris-Glycine gradient gel (Invitrogen, Carlsbad, CA) followed by transfer to a PVDF membrane. The resulting membrane was stained with Coomassie Brilliant Blue R-250 stain (TekNova, Hollister, CA), rinsed with 50% methanol until the protein band resolved, and air dried. Proteolytic fragments were sequenced according to the Edmans' protocol by the UC Davis Molecular Structure Facility to determine the cleavage sequences. Table 25 below depicts the protease cleavage sequences of human C2, C3, and C4. Where cleavage occurred, the respective cleavage sites on C2, C3 and C4, as identified from sequencing of the cleavage products, are shown for the natural protease Factor I, cathepsin K, MT-SP1, and modified MT-SP1 (CB155). The respective SEQ ID NOS are indicated in parentheses next to the sequence.

Table 25: Protease Cleavage Sequences

		MT-SP1	CB155	Cathepsin K	Factor I
Human C2		GATR (391) SLGR (392) VFAK (393)	GATR (391) SLGR (392)		
Human C3	**Beta chain**		REFK (394)		
	Alpha chain	GLAR (395) RLGR (396) AEGK (397)	QHAR (398)	LGLA (399) LSVV (400)	LPSR (388) SLLR (389)
Human C4	**Beta chain**				
	Alpha chain	HRGR (390)			HRGR (390)
	Gamma chain				

Example 12

Correlation of C2 Cleavage with Complement Inactivation: Assessment of the Formation of C3 Convertase and Hemolysis

C3 convertase is formed by the interaction of C1 complex with C4 and C2. Activation of the C1r protease in the C1 complex cleaves C1s yielding an active C1s protease. C4 is a sensitive substrate for C1s, thereby resulting in cleavage of C4 into C4a and C4b. The generation of an active C4b provides a binding site for C2, a second substrate for C1s. Cleavage of C2 results in the formation of fragments C2a and C2b. Upon cleavage by C1s, the C4b and C2b fragments become associated, which together form the C3 convertase of the classical pathway. The SLGR cleavage

site present in C2 is the natural activation site for C2 cleavage yielding C2a and C2b, whereas the VFAK cleavage sequence in C2 is present within the protease domain of C2 in the C2a portion of the molecule. To assess whether cleavage of cleavage sequences in C2 by wildtype or modified MT-SP1 affects activation of C2 and the formation of C3 convertase, cleavage was assessed and the functional consequences of cleavage was determined in an *in vitro* reconstituted cell surface hemolysis model.

A. C2 cleavage

The presence of C2a and C2b cleavage products was assessed after cleavage of purified C2 by wildtype MT-SP1 (CB200), CB252, or CB377. To assess cleavage products upon incubation of purified C2 with proteases, 5 μg of purified C2 (Quidel) was incubated alone or with a final concentration of 100 nM CB200, CB252, or CB377 protease for 1 hour at 37° C. The entire reaction was separated by SDS-PAGE on a 4-12% Tris-Glycine gradient gel (Invitrogen, Carlsbad, CA) followed by transfer to a PVDF membrane. The resulting membrane was stained with Coomassie Brilliant Blue R-250 stain (TekNova, Hollister, CA), rinsed with 50% methanol until the protein band resolved, and air dried. The results show that in the presence of 100 nM CB200, CB252 or CB377, C2 was almost completely degraded to yield cleavage products of about 70 kD and 23 kD corresponding to C2a and C2b, respectively. In addition, in the presence of CB200 a third cleavage product of about 35 kD was observed.

B. Cell Surface Hemolysis Model

The activity of MT-SP1 or modified protease on the C2 protein specifically was assayed by isolating cells in the intermediate stages of complement activation and exposing them to plasma or protein treated with the protease. Briefly, activated erythrocytes were stopped at the C1/C4b complex stage using the method of Nagaki *et al* (1974, A New Method for the Preparation of EAC14 cell with Human or Guinea-Pig Serum. *Journal of Immunological Methods* 5:307-317.) Purchased activated erythrocytes (Diamedix Corp) were washed three times by pelleting the cells at 2000 rpm followed by resuspension into GGVB-TTHA (50% GVB^0 (Diamedix Corp.) + 5% glucose + 5 mM Ca-TTHA (equal parts of 100 mM $CaCl_2$ with 100 mM TTHA (Sigma)), and after the final wash were resuspended at 5 X 10^8 cells/mL and stored on

ice. The cells were mixed with 2.5 volumes of 10% normal human serum (NHS; made in GGVB-TTHA and incubated 15 minutes at 30°C to ensure the chelation of Mg^{2+}) and incubated for 5 minutes at 30°C. The mixture was washed two times with GGVB-TTHA, washed two times with GGVB-Ca (50% GVB^0 + 5% glucose + 0.3 mM $CaCl_2$), and washed two times with GGVB++ (50% GVB^0 + 5% glucose + 1 mM $MgCl_2$ + 0.15 mM $CaCl_2$). After the final wash, the cell mixture was incubated 2 hours at 37°C with mixing every 30 minutes to avoid excess settling of the cells. The incubated cell mixture was washed one time in GGVB++, and resuspended at 1.5 X 10^8 cells/mL. The suspension was stored up to 1 week at 4°C.

During complement activation, the C1/C4b complex is required to cleave C2 generating C3 convertase and the resultant activation of the remainder of the complement cascade resulting in the formation of the membrane attack complex (MAC) and cell lysis. To assess the consequences of C2 cleavage by protease, a 2X protease solution of any of CB200, CB252, CB377 was serially diluted by diluting a stock solution of the protease to 2 μM in GGVB++ and serially diluting this stock 1:2 across 11 wells of an opaque 96 well assay plate (Nunc) for final protease concentrations of 0.2 nM to 2000 nM. GGVB++ buffer alone was added to the 12th well as a background control. A 40% solution of C3 depleted sera (Sigma) was made by dilution with GGVB++. Five microliters of serially diluted 2X protease (from above) was mixed with 5 μL diluted C3-depleted sera and incubated for 1 hour at 37°C. The reaction was diluted to 50 μL with GGVB++ and 50 μL EAC14b cells (at 1.5 X 10^8 cells/mL) were added. The mixture was incubated for 6 minutes at 30°C to pre-form the C2 complex. 150 μL C2 depleted sera, diluted 1:100 in GGVB-EDTA (50% GVB^0 + 5% glucose + 10 mM EDTA), was added to each well. Samples were incubated 1 hour at 37°C with gentle shaking. The plate was spun at 2000 rpm to pellet the cells and 100 μl of the supernatant was transferred into a clear 96 well assay plate. Release of hemoglobin from the lysed red blood cells was monitored by reading the optical density (OD) at 415 nm.

The results show that C3 depleted sera pre-incubated with increasing concentrations of proteases (CB200, CB252, or CB377) conferred reduced hemolysis of erythrocytes containing preformed C1/C4b when added to sera depleted for C2.

The affects of each of the tested proteases was dose-dependent with little to no inhibition evident at concentrations ranging from 0.2 nM to 10 nM of protease, with successive inhibition occurring at increasing protease concentrations with little to no hemolysis observed at protease concentrations of 800 nM or more. These results suggest that preincubation of sera containing C2 in the presence of proteases does not mimic cleavage of C2 by C1/C4b required for complement activation and cell lysis.

Example 13

Determination of the Inhibitory Cleavage Site by Paired SDS-PAGE and Hemolytic Assays

To correlate protease cleavage of complement components with inhibition of complement activation, purified complement factors were purchased from Quidel and CompTech. 5 μg of each protein was diluted to a final concentration of 5 μM in PBST. A scaffold or modified protease was diluted to a final concentration between 0 and 500 nM. Samples were incubated for 1 hour at 37°C. 0.5 to 1 μg of the treated complement component was removed and diluted to a total volume of 10 μl with PBST. This reaction was mixed with 250 μl IgG-activated sheep's red blood cells and 5 μl media depleted of the corresponding complement factor to be assayed. The solution was allowed to incubate at room temperature for 45 minutes. The cells were spun down at 5000 rpm for 2 minutes and 200 μl of the supernatant was transferred to a 96-well microtiter plate and absorbance at 415 nm was measured to determine release of hemoglobin from the lysed red blood cells.

The remaining 4 to 4.5 μg of the reaction sample was deglycosylated according to the manufacturer's protocol for PNGaseF (New England BioLabs). The samples were separated by SDS-PAGE on a 4-12% Tris-Glycine gradient gel followed by staining with Coomassie Brilliant blue stain. Using the densitometry feature on an Alpha Innotech Imager, the area of each band was determined and used to calculate the percentage of the full length complement component cleaved throughout the assay and the appearance of all major degradation products.

Example 14

Correlation of C2 Cleavage with Complement Inactivation as Assessed by Hemolysis in C2 Depleted Sera

The functional consequence of C2 cleavage of complement-mediated hemolysis was assessed in a paired SDS-PAGE and hemolytic assay as described above in Example 13. To assess complement activation by purified complement factors, purified C2 and C2-depleted media were purchased from Quidel. 0.5 to 1 μg of purified C2 was incubated with 10 to 500 nM CB155 protease in a total of 10 μl PBST for 1 hour at 37°C. The entire reaction was added to 250 μl of IgG-activated sheep's red blood cells along with 5 μl of plasma depleted of the C2 complement factor being assayed. The solution was allowed to sit at room temperature for 45 minutes. The cells were spun down at 5000 rpm for 2 minutes and 200 μl of the supernatant was transferred to a 96-well microtiter plate and absorbance at 415 nm was measured to determine release of hemoglobin from the lysed red blood cells.

To visualize the proteolytic cleavage products, twenty microliters of the reaction, or purified complement C2 as a control (CompTech), was separated by SDS-PAGE on a 4-12% Tris-Glycine gel and total protein was visualized by staining the gel with Coomassie Blue according to the manufacturer's protocol. The cleavage of C2 was compared using gel densitometry. Cleavage of C2 occurred in a dose-dependent manner with almost complete cleavage of C2 occurring at 500 nM of protease. Further, the percent hemolysis decreased with increasing concentrations of the protease. The IC_{50} of CB155 based on gel densitometry of C2 cleavage products was 2.2 nM. The IC_{50} of CB155 for hemolysis in C2 depleted serum supplemented with protease-treated C2 was 17 nM. *In vitro*, complete degradation of purified C2 is required for the functional decrease in hemolysis.

Example 15

Detection of C5b-9 (Membrane Attack Complex) by ELISA and Effects of MT-SP1 or Mutants on Complement Activation

A. C5b-9 ELISA

ELISAs for C5b-9 were performed according to the manufacturer's protocol (Quidel). Briefly, microtiter plates coated with the capture antibody were rehydrated with SuperBlock (Pierce, Rockford, IL) for 30 minutes at room temperature. The plates were washed in PBST and 20 μl of the protease-treated, complement stimulated serum solution from above diluted with 80 μl SuperBlock was added to wells of a

microtiter plate. The plates were incubated at room temperature for 1 hour and then washed in PBST. 100 µl of the detection antibody-HRP conjugate solution was added and the plates were incubated for 1 hour and then washed in PBST. Finally, 100 µl of the substrate solution was added and the plates were incubated about 15 minutes at room temperature to develop. To stop the developing reaction, 100 µl of stop solution was added to each well and absorbance at 450/650 nm was measured according to the manufacturer's protocol.

B. Effects of wildtype MT-SP1 (CB200), CB155 or CB42 on complement activation

To detect complement activation, human plasma with sodium citrate as an anticoagulant (Innovative Research, Inc., Southfield, MI) was diluted into PBS with 0.05% Tween 20 (PBST) to a final concentration of 20% (10 µl serum in 40 µl PBST), to which wildtype MT-SP1, CB155, or CB42 were added to a final concentration of 0-5 µM. The solution was incubated at 37°C for 15 minutes. Activation of the classical pathway and activation of the alternative pathway was initiated by the addition of lipopolysaccharide (IgG or LPS, respectively at 1 mg/ml final concentration, Sigma). The reaction was incubated at 37°C for 30 minutes. The reaction was quenched by adding Pefabloc (Roche) to a final concentration of 1 mg/ml and EDTA to a final concentration of 50 mM. 20 µl of the final solution was used for the subsequent ELISA. The ELISA was performed as described in part A above.

The IC50 of C5b-9 generation for each of the proteases was determined. The IC_{50} following activation of the classical pathway for wildtype MT-SP1, CB155, and CB42 was determined to be 103 nm, 47 nm, and 23 nm, respectively. The IC_{50} following activation of the alternative pathway for wildtype MT-SP1, CB155, and CB42 was determined to be 195 nm, 84 nm, and 41 nm, respectively.

Example 16
Effects of wildtype MT-SP1 (CB200), CB252 or CB377 on complement activation In a Total Complement System Screen

To assess the affect of MT-SP1 or mutant MT-SP1 proteases on the classical, MBL, or alternative complement pathways, 9 µl of human citrated plasma (Innovative Research) was incubated with 1 µl of CB200, CB252, or CB377 protease to give a

final concentration of 1 μM of protease for 1 hour at 37°C. Each of the reactions were assessed for complement activation using the Total Complement System Screen Classical, Lectin, Alternative Pathways, according to the protocol from the manufacturer (WiesLab; Sweden). In this assay, the wells of the microtiter strips provided by the manufacturer are coated with specific activators of the classical, alternative, or MBL (lectin) pathways. The reaction was diluted into the appropriate buffer provided by the manufacturer to give the concentration of plasma for each pathway and the reaction was incubated as defined by the manufacturer. For the classical pathway, the plasma sample was diluted in Dilutent CP and left at room temperature for a maximum of 60 minutes before analysis. For the lectin pathway, the plasma sample was diluted in Diluent LP and incubated at room temperature for greater than 15 minutes but less than 60 minutes before analysis. For the alternative pathway, the plasma sample was incubated in Diluent AP and left at room temperature for a maximum of 60 minutes before analysis. To the microtiter plate, samples were added at 100 μl/well in duplicate. The plate was incubated for 60-70 minutes at 37°C. After the serum incubation, the wells of the microtiter plate were washed three times with 300 μl washing solution. After the final wash, excess wash buffer was removed by tapping the plate on an absorbent tissue. Complement activation was assessed in each sample by detection of C5b-9. 100 μl of the conjugate contain alkaline phosphatase-labelled antibodies to C5b-9 was added to each well and the plate incubated for 30 minutes at room temperature. To develop the reaction, 100 μl substrate solution was added to each well and the plate incubated at room temperature for 30 minutes. The reaction was stopped by adding 5 mM EDTA at 100 μl/well. The absorbance was read at 405 nm using a microplate reader. The fraction of sC5b-9 generated was determined by comparing the OD405 value of the sample to a no protease control sample.

The results show that the fraction C5b-9 generated upon complement activation induced by the classical and MBL pathways was almost completely inhibited in the presence of each of the tested proteases (CB200, CB252, or CB377). In contrast, little to no inhibition of C5b-9 generation was observed by any of the tested proteases when complement activation was induced by the alternative pathway.

Since the classical and MBL pathways require C2, but the alternative pathway does not, these results suggest that inhibition of the classical and MBL pathways is due to cleavage of C2. This result is consistent with the observation that each of the tested proteases (CB200, CB252, and CB377) when preincubated with C2 inhibit hemolysis (see Example 8.b above).

Example 17

Screening for preferential cleavage of SLGR or GLAR versus RQAR substrates

Modified proteases that match the desired specificity profiles, as determined by substrate libraries, were assayed using individual peptide substrates corresponding a desired cleavage sequence to determine the magnitude change in specificity. One native target substrate was designed: Ac-RQAR-AMC, which includes the MT-SP1 auto-activation site; and two desired substrate cleavage sequences were designed: Ac-SLGR-AMC (C2 cleavage site) and Ac-GLAR-AMC (C3 cleavage site).

The substrates were diluted in a series of 12 concentrations between 1 mM and 2 μM in 50 μl total volume of MT-SP1 activity buffer in the wells of a Costar 96 well black half-area assay plate. The solution was warmed to 30° C for five minutes, and 50 μl of a protease solution (wildtype MT-SP1, CB42, or CB155) was added to the wells of the assay. The fluorescence was measured in a fluorescence spectrophotometer (Molecular Devices Gemini XPS) at an excitation wavelength of 380 nm, an emission wavelength of 450 nm and using a cut-off filter set at 435 nm. The rate of increase in fluorescence was measured over 30 minutes with readings taken at 30 second intervals. The kinetic constants k_{cat}, K_m, and k_{cat}/K_m (specificity constant) were calculated by graphing the inverse of the substrate concentration versus the inverse of the velocity of substrate cleavage, and fitting to the Lineweaver-Burk equation ($1/velocity=(K_m/V_{max})(1/[S]) + 1/V_{max}$; where $V_{max}=[E]*k_{cat}$). The proteases wildtype MT-SP1 (CB200), CB42, and CB155 cut the Ac-RQAR-AMC substrate at 1.9×10^6, 1.8×10^6, and 9.1×10^4 $M^{-1}s^{-1}$, respectively. The proteases wildtype MT-SP1 (CB200), CB42, and CB155 cut the Ac-SLGR-AMC substrate at 2.0×10^4, 5.9×10^4, 3.7×10^3 $M^{-1}s^{-1}$, respectively. The proteases wildtype MT-SP1 (CB200), CB42, and CB155 cut the Ac-GLAR-AMC substrate at 6.4 X104, 6.3 X104, and 3.5 X 103 $M^{-1}s^{-1}$, respectively.

Example 18

Screening for cleavage of individual substrates versus a full-length protein

The specificity of a wildtype or modified protease to a substrate cleavage sequence versus a full length complement protein was determined by comparing the specificity constant (k_{cat}/k_m) to measure how well a substrate is cut by a particular protein. A peptide substrate cleavage sequence was designed containing a C2 cleavage sequence: Ac-SLGR-AMC. The specificity constant (k_{cat}/ K_m) of cleavage was determined as described above in Example 17 by incubating the substrate cleavage sequence with a protease (wildtype MT-SP1 (CB200), CB42, or CB155) and the rate of increase in fluorescence was determined.

In gel kinetics was used to determine the specificity constant of the target complement protein C2. The kinetics of cleavage of the C2 target protein was assayed by following by SDS-PAGE the depletion of the target in the presence of a small amount of protease over a time course. For this assay, 5 mM C2 was incubated with 10 nM protease (wildtype MT-SP1 (CB200), CB42, or CB155) in MTSP activity buffer at 37°C for 5 hours. Aliquots were removed at 0, 10, 20, 40, 60, 100, 200 and 300 minutes, and immediately diluted and boiled in reducing agent. The samples were treated with PNGase F (New England BioLabs), separated by SDS-PAGE, and stained with Coomassie Brilliant Blue. The density of the full length protein band was determined using the Alpha Innotech Gel Imager. The specificity constant, k_{cat}/K_m was determined by non-linear fitting of the curve produced by plotting the integrated density value versus time with the equation:

density = exp (-1*time*[enzyme]*kcat/Km).

The results show that the specificity constant of cleavage of a substrate peptide sequence versus a full length protein by the proteases followed a similar pattern. The CB200 wildtype MT-SP1 showed almost identical specificity constants for cleavage of the substrate peptide sequence versus the C2 full length protein, whereas CB42 and CB155 showed slight variation in their specificity constants. The specificity constant of cleavage of the Ac-SLGR-AMC substrate sequence by CB200, CB42, and CB155 was 2.0×10^4, 5.9×10^4, and $3,7 \times 10^3$ $M^{-1}s^{-1}$, respectively. The specificity constant

of cleavage of the C2 protein by CB200, CB42, and CB155 was 1.95 X 10^4, 3.60 X 10^4, and 7.20 X 10^4 $M^{-1}s^{-1}$, respectively.

Example 19
Cynomolgus Hemolysis Protocol

The functional activity of the Cynomolgus monkey complement system following protease treatment also can be assessed using modified hemolytic assays.

A. Sensitization of chicken red blood cells

Chicken red blood cells were isolated from Chicken Alsevers (50% mix of whole blood from chickens and alsevers solution, which contains anti-coagulants; Colorado Serum Company, CO). The cells were resuspended by gently pipetting up and down until no cell pellet was visible and 50 µl of cells were diluted into 1 ml GVB++ buffer. The volume of cells was scaled as necessary for each experiment assuming that 10 µl per well of the final 1 ml suspension would be added to each well so that a dilution of 50 µl cells was sufficient for one plate. The cells were washed by pelleting the cells at 2500 rpm in a tabletop centrifuge at 4°C for 1 minute, the supernatant discarded, and cells resuspended in 1 ml GVB++ by gently pipetting up and down. The washing steps were repeated twice more or until the supernatant was completely clear upon the last spinning. One µl of anti-chicken erythrocyte antibody (Fitzgerald industries) was added to sensitize the cells. After the antibody – cell suspension was mixed, the solution was incubated on ice for a minimum of 15 minutes, then centrifuged at 2000 rpm in a tabletop centrifuge at 4°C for 2 minutes. The supernatant was discarded and the sensitized cells were resuspended in 1 mL GVB++ and washed a further 2 times by centrifugation at 2000 rpm for 1 minute until the supernatant was clear. After the final wash, the cell pellet was resuspended in a final volume of 1 ml GVB++ and the cells were diluted 10:50 in GVB++ (*i.e.* 1 ml of resuspended sensitized cells 5 mL GVB++ for a total volume of 6 ml). Sensitization of the chicken cells with antibody was performed fresh the day of the experiment. The sensitized cells were not kept overnight.

B. Hemolysis assay from in vivo pharmacodynamic (PD) experiments

Hemolysis reactions were set up at a final concentration of 1%, 2.5%, and 10% plasma for each plasma sample obtained from protease treated animals or vehicle

control (no protease) treated animals in the presence of sensitized erythrocytes. Absorbance controls containing no added concentrated sensitized erythrocytes also were set up in parallel for each sample. All reactions were set up in opaque plates with point divots. For the 1% plasma samples, the hemolysis samples (in duplicate) were set up with 10 µl sensitized erythrocytes, 89 µl GVB++, and 1 µl plasma from protease or no-protease treated animals; and the corresponding absorbance controls were set up with 99 µl GVB++ and 1 µl of plasma from protease treated animals. For the 2.5% plasma samples, the hemolysis samples (in duplicate) were set up with 10 µl sensitized erythrocytes, 87 µl GVB++ and 2.5 µl plasma from protease or no protease treated animals; and the corresponding absorbance controls were set up with 97 µl GVB++ and 2.5 µl plasma from protease treated animals. For the 10% plasma samples, the hemolysis samples (in duplicate) were set up with 10 µl sensitized erythrocytes, 80 µl GVB++, and 10 µl plasma from protease or no protease treated animals; and the corresponding absorbance controls were set up with 90 µl GVB++ and 10 µl plasma from protease treated animals. The plates were incubated with shaking at 37°C for 30 minutes. The cells were centrifuged at 2000 rpm for 5 minutes to pellet the unbroken cells, and 80 µl of the supernatant was removed and placed in a clear 96-well round-bottom microtiter plate. This was done carefully since the samples were sometimes gelatinous. The samples that were gelatinous were noted. The supernatant-transferred plates were centrifuged at 2500 rpm for 5 minutes to remove bubbles. Centrifugation was repeated until no bubbles persisted or, alternatively, remaining bubbles were popped with an 18G needle. Release of hemoglobin from the lysed red blood cells was monitored photometrically by reading absorbance at 415 nm on a Bio-Rad Microplate Reader Model 680. If the absorbance was greater than 1, the samples were diluted 1:3 in GVB++ and read again (i.e. 20 µl sample into 40 µl GVB++). The fraction hemolysis was calculated by subtracting the absorbance from the absorbance control samples from the corresponding hemolysis well, then dividing the experimental samples by the no-protease vehicle control sample. ED50 values were determined by graphing the OD415nm value as a function of protease concentration.

C. ***In vitro* titration hemolysis assay**

For an *in vitro* titration of proteases using cynomolgus monkey plasma, proteases at 10% of the final reaction volume were incubated with purchased cynomolgus monkey plasma (*i.e.* in polypropylene 96-well plates, 2 µl of the protease solution was added to 18 µl cynomolgus monkey plasma) to give final protease concentrations of protease of ranging from 20 µM to 0.156 µM for the IC_{50} titration protocol, and a plasma concentration of 90%. A no-protease (18 µl plasma and 2 µl GVB/Mg/EGTA) and background (20 µl GVB/Mg/EGTA only) controls also were included in the assays. The reaction was incubated at room temperature for 1 hour. After preincubation of the protease with 90% plasma, hemolysis was performed as described in part B above. No absorbance controls were included in the in vitro hemolysis titration.

Example 20
Mouse Hemolysis Protocol

A. Hemolysis assay from in vivo pharmacodynamic (PD) experiments

The functional activity of the mouse complement system following protease treatment also can be assessed using modified hemolytic assays. Erythrocytes used in the mouse hemolysis protocols also were chicken red blood cells which were sensitized as described in Example 19, part A above. Hemolysis reactions were set up at a final concentration of 40% plasma for each plasma sample obtained from protease treated animals or vehicle control (no protease) treated animals in the presence of sensitized erythrocytes. Absorbance controls containing no added concentrated sensitized erythrocytes also were set up in parallel for each sample at half the plasma concentration (20% plasma), such that the absorbance control values were subtracted twice from the hemolysis values during analysis as discussed below. The hemolysis samples were set up in duplicate (if enough plasma allowed) in opaque plates with divots by adding 60 µl of concentrated sensitized erythrocytes and 40 µl of plasma from protease or no protease treated animal to each well. The corresponding absorbance control was set up by adding 80 µl GVB++ and 20 µl mouse plasma from protease or no protease treated animals to each well. The plates were incubated with shaking at 37°C for 1 hour. The cells were centrifuged at 2000 rpm for 5 minutes to pellet the unbroken cells, and 50 µl of the supernatant was removed and placed in a

clear 96-well round-bottom microtiter plate. This was done carefully since the samples were sometimes gelatinous. The samples that were gelatinous were noted. The supernatant-transferred plates were centrifuged at 2500 rpm for 5 minutes to remove bubbles. Centrifugation was repeated until no bubbles persisted or, alternatively, remaining bubbles were popped with an 18G needle. Release of hemoglobin from the lysed red blood cells was monitored by reading at 415 nm. If the absorbance was greater than 1, the samples were diluted 1:3 in GVB++ and read again (i.e. 20 µl sample into 40 µl GVB++). The fraction hemolysis was calculated by subtracting the 2X absorbance absorbance control samples from the corresponding hemolysis well, then dividing the experimental samples by the no-protease vehicle control. ED50 values were determined by graphing the OD415nm value as a function of protease concentration.

B. *In vitro* titration hemolysis assay

For an *in vitro* titration of proteases using mouse plasma, proteases at 10% of the final reaction volume were incubated with purchased mouse plasma or in-house control plasma (*i.e.* in polypropylene 96-well plates, 2 µl of the protease solution was added to 18 µl plasma) to give final protease concentrations of protease of ranging from 20 µM to 0.156 µM for the IC_{50} titration protocol, and a plasma concentration of 90%. A no-protease (18 µl plasma and 2 µl GVB/Mg/EGTA) and background (20 µl GVB/Mg/EGTA only) controls also were included in the assays. The reaction was incubated at room temperature for 1 hour. After preincubation of the protease with 90% plasma, hemolysis was performed as described in part A above. No absorbance controls were included in the *in vitro* hemolysis titration.

Example 21

Classical C3b Deposition ELISA

To detect and quantitate C3b deposition, 96 well Maxisorp plates (Nunc) were coated with 100µl/well of 0.5% ovalbumin for 2hrs at 37°C or overnight at 4°C. The plates were washed 3 times with 250 µl PBST using a Molecular Devices SkanWasher 300 Version B. The plates were coated with 100 µl/well of rabbit anti-chicken egg albumin antibody (MP Biomedicals) diluted 1:1000 in PBS. The plates were incubated for 1 hr at room temperature or overnight at 4°C before being washed

3 times with PBST. The plates were blocked with 200 µl Blocking Buffer (30% BSA Solution; Serologicals), and the plates were shaken at room temperature for 1 hour. After washing 3 times with PBST, 100 µl of plasma sample, diluted to the desired percentage (*i.e.* 1%, 10%) in GVB++ (Veronal (barbital)-buffered saline, pH 7.4, containing 142 mM NaCl, 4.9 mM sodium Veronal, 0.1% gelatin, 0.15 mM $CaCl_2$, and 1 mM $MgCl_2$; Comptech), was added to each well, and the plates were shaken at room temperature for 30 minutes. The wells were washed 3 times with PBST. Goat anti-human C3b antibody (Quidel) diluted 1:4000 in blocking buffer was added to the wells at a volume of 100 µl, and the plates were shaken at room temperature for 1 hour. After washing with PBST, 100 µl HRP-rabbit anti-goat conjugated antibody (Zymed) diluted 1:8000 in blocking buffer was added to the wells and allowed to incubate for 1 hour with shaking at room temperature. The wells were washed with PBST and the ELISA was developed according to the manufacturers instructions by the addition of 100 µl TMB substrate (Pierce). The reaction was stopped by the addition of 100 µl 2M H_2SO_4 and the absorbance at 405 nm was read on a SpectraMax M5 plate reader (Molecular Devices).

EXAMPLE 22
Mouse Pharmacodynamic (PD) Analysis of Protease

A. Pharmacodynamics of CB450

Mice (n=6 for each dose) were injected intravenously with a bolus of CB450 at varying dosages ranging (0 mg/kg, 2.5 mg/kg, 5 mg/kg, 10 mg/kg, and 15 mg/kg). Plasma was collected from the treated mice at 5 minutes post-injection by cardiac puncture. Complement activity of the plasma samples from the different treatment groups were tested by hemolysis assay as described in Example 20 or by C3b deposition as determined by a C3b ELISA described in Example 21.

The results of the hemolysis experiment showed that there was a dose-dependent decreased hemolysis of erythrocytes induced by mouse plasma from CB450 treated mice as assessed by absorbance levels at 415 nm. Plasma samples from mice treated with no protease induced hemolysis in this assay as assessed by an absorbance at 415 nm of about 0.23, which decreased to about 0.1 in the 2.5 mg/kg

CB450 treatment group with little to no detectable absorbance signal measured in samples from mice treated with 5, 20, or 15 mg/kg of CB450.

The C3b ELISA was performed using 1% or 10% plasma from each of the treatment groups. The fraction hemolysis from the no protease treated sample was set at 1.0 and the fraction hemolysis of all experimental samples was accordingly determined. Thus, for both the 1% and 10% plasma samples from mice treated with no protease, the fraction of C3b deposition was measured to be 1. The results of the C3b ELISA on the 10% plasma samples showed that the plasma from mice treated with increasing doses of CB450 showed no measurable difference in C3b levels at doses of CB450 of 2.5, 5, or 10 mg/kg as compared to the no protease treated sample, however, mice treated with 15 mg/kg exhibited a decreased fraction of C3b deposition which was measured to be about 0.40. The results of the C3b ELISA on the 1% plasma samples showed that plasma from mice treated with CB450 had a dose-dependent decrease in the fraction C3b deposition as compared to the no protease treated plasma sample, which was consistent with the results observed in the hemolysis experiment. Plasma samples from mice treated with 2.5 mg/kg CB450 exhibited a decreased C3b deposition which was measured to be about 0.40, while plasma from mice treated with 5, 20, or 15 mg/kg CB450 showed little to no detectable C3b.

B. Pharmacodynamics of a Panel of MT-SP1 Protease Mutants

Mice were injected intravenously with a bolus of increasing concentrations of a panel of MT-SP1 mutants including CB200 (wild-type), CB238, CB245, CB252, CB255, CB257, CB268, CB351, CB377, CB409, CB422, CB450, CB464, and CB473. Plasma was collected from the treated mice at 5 minutes post-injection by cardiac puncture. Complement activity of the plasma samples from the different treatment groups were tested by hemolysis assay as described in Example 19 or by C3b deposition as determined by a C3b ELISA (assayed in 1% and 10% plasma) as described in Example 20. The results were graphed as a function of protease concentration to determine the ED50 values. A summary of the results are depicted in Table 26 below. The Table also sets forth the maximum tolerated dose (MTD) of

protease and the therapeutic index (TI) calculated as the ratio of MTD to ED50. The results show differences in the *in vivo* efficacy of some of the tested proteases.

TABLE 26: Mouse Pharmacodynamics

PROTEASE	MTD (mg/kg)	Hemolysis (ED50; mg/kg)	Hemolysis TI	C3b in 1% plasma (ED50; mg/kg)	C3b TI (1 % plasma)	C3b in 10 % plasma (ED50; mg/kg)	C3b TI (10% plasma)
CB200	10	6.4	1.56	2.7	3.7	13.5	0.74
CB238	15	9.4	1.6	6.1	2.46	16.2	0.92
CB245	10	2.4	4.1	2.63	3.8	>10	0
CB252	12.5	5.7	2.19	3.8	3.29	9.9	1.26
CB255	7	5	1.4	2.78	2.52	>7	0
CB257	5	3.1	1.6	4.86	1.03	>5	0
CB268	10	9.9	1	5.45	1.8	>10	0
CB351	10	6.6	1.52	5.8	1.72	10.8	0.93
CB377	15	8.6	1.75	2.6	5.77	6.2	2.42
CB409	15	8.2	1.8	3.2	4.65	17.99	0.83
CB422	12.5	10.25	1.22	3.82	3.27	20.36	0.61
CB450	15	1.8	8.5	3.5	4.3	15.9	0.9
CB464	15	7.72	1.94	5.07	2.96	33.1	0.45
CB473	12.5	14.25	0.86	1.95	6.41	8.01	1.56

EXAMPLE 23
Rat Pharmacodynamic (PD) Analysis of Protease

A. CB252 and CB377

Rats were injected intravenously with a bolus of CB252 (23 mg/kg) followed by infusion for 1 hour at 3.3 mg/kg/hr or with a bolus of CB377 (18 mg/kg) followed by infusion for 1 hour at 1.8 mg/kg/hr. Rats treated with a vehicle control also were included in the study. Plasma was collected at various time points after injection (where t=0 is pre-injection; i.e. 0, 5, 15, 30, 60, or 120 minutes) and analyzed for complement activity by assaying for C2 cleavage by Western Blot as set forth in Example 9 (except that only 1.5 µl of plasma was used) and for hemolysis using the

Cynomolgus hemolysis protocol as set forth in Example 19 using either 1% or 10% rat plasma.

The results showed increased cleavage of C2 in plasma from CB252 and CB377 treated rats. CB252 showed a greater cleavage of C2 as there was little detectable C2 present in the plasma samples as assessed by Western Blot even after only 5 minutes following injection, with no detectable C2 present at 60 or 120 minutes after injection. CB377 also showed diminished C2 levels as compared to vehicle control at early time points, however, by 60 minutes and 120 minutes the levels of C2 were comparable to those from vehicle control samples.

The results of hemolysis induced by 10% plasma from the treated rats showed that plasma from CB377 had no effect on the inhibition of hemolysis as compared to vehicle control, while plasma from CB252 showed a marked inhibition of hemolysis. Plasma samples from rats treated with CB252 collected at 5, 15, 30, and 60 minutes after injection showed little to no detectable hemolysis. Hemolysis was increased to levels comparable to vehicle control by plasma from CB252 treated mice at later time points (*i.e.* by 90 and 120 minutes). The effects of CB252 and CB377 was more pronounced when hemolysis was induced by 1% plasma from each of the treated rats. The fraction hemolysis (set at 1.0 for the t-=0 time point vehicle control sample) induced by 1% plasma from vehicle control rats did not change among the tested time points and was always around about 1.0. Plasma from rats treated with CB252 induced no detectable hemolysis at any of the collected time points. Plasma from CB377 treated rats also showed reduced hemolysis as compared to plasma from vehicle control treated animals at all time points, although to a lesser extent than plasma from CB252 treated rats. Hemolysis was reduced to the greatest extent in plasma collected 15 minutes after injection of CB377 with a reported fraction of hemolysis of about 0.2 as compared to plasma control treated mice, and steadily increased at longer time points after injection to about 0.6 at 120 minutes after injection.

B. Comparison of CB200, CB155, and CB42

Rats were injected intravenously with a bolus of CB200 (wildtype), CB155, and CB42 at 2 mg/kg, 10 mg/kg, and 25 mg/kg. Plasma was collected at various time

points after injection (where t=0 is pre-injection) up to about 1380 minutes after injection and analyzed for complement activity by assaying for hemolysis using the Cynomolgus hemolysis protocol as set forth in Example 19 using 1% plasma. The results show that plasma from rats treated with CB200 or CB42 at 2 mg/kg and 10 mg/kg exhibited levels of hemolysis comparable to levels observed at t=0 before pre-injection of the protease. Plasma from rats treated with 25 mg/kg of CB200 or CB42 induced reduced hemolysis of erythrocytes at early time points, with little to no hemolysis observed at time points up to about 60 minutes after injection of the protease. Hemolysis was increased to levels comparable to hemolysis at t=0 before pre-injection of the protease from plasma samples collected by 1380 minutes after injection of CB200 or CB42. Plasma from CB155 treated rats, however, showed decreased hemolysis at all doses tested. Treatment of rats with 2 mg/kg or 10 mg/kg showed slight but reproducibly decreased hemolysis induced by plasma collected at early time points as compared to t=0 before pre-injection of the protease. Plasma samples collected at about 30 minutes after rats receiving a dosage of 2 mg/kg or 10 mg/kg of CB155 resulted in an observed OD415 of hemolysis of about 0.3 or about 0.25, respectively, as compared to about 0.45 for t=0 (no protease) plasma samples. Plasma collected at 240 minutes or longer after preinjection of CB155 at 2 mg/kg and 10 mg/kg induced hemolysis to levels comparable to that observed from t=0 treated animals. Plasma from rats treated with 25 mg/kg of CB155 induced reduced hemolysis of erythrocytes at early time points, with little to no hemolysis observed at timepoints up to about 240 minutes after injection of the protease. Hemolysis was increased to levels comparable to hemolysis at t=0 before pre-injection of the protease from plasma samples collected by 1380 minutes after injection of CB155. These results show that CB155 has a greater *in vivo* pharmacodynamic efficacy on complement inactivation than do CB200 and CB42 as assessed in this experiment.

EXAMPLE 24

Cynomolgus Monkey Pharmacodynamic (PD) Analysis of Protease

A. CB252 Cynomolgus *ex vivo* Complement Inhibition

Two naive male and two naive female cynomolgus monkeys (approximately 2.2 – 4.4 kg, and 2-4 years of age at initiation of treatment) were assigned to a single treatment group. Each animal was permanently tattooed with a unique identification

number and assigned to a 14-day acclimation period prior to dosing. Study animals were intravenously administered 1 and 3 mg/ml doses of CB252 at volumes of 5 mg/kg. Blood samples for ex vivo pharmacodynamic analyses were collected at scheduled time points (Pre-injection, i.e. t=0; 5 minutes, 30 minutes, and 60 minutes post-injection). Blood was collected by venipuncture from a peripheral vein of restrained, conscious animals. Blood samples were collected from spare animals to be used as baseline values. Approximately 1 ml of blood was transferred to a tube treated with lithium heparin, placed on ice, and then centrifuged at 2000 g for 15 minutes at 4° C within 30 minutes of collection. Plasma obtained was divided into two approximately equal aliquots and then transferred to cyrovials which were frozen on dry ice. Samples were stored at approximately -60° C or colder prior to thawing and analysis. Plasma samples were tested for effects on complement activation by assaying for C2 cleavage by Western Blot, C3b deposition by ELISA at 1% and 10% plasma concentration, and through hemolysis of sensitized chicken red blood cells at 1%, 2.5%, and 10% plasma.

1. C2 cleavage

C2 cleavage in the plasma samples was assessed by Western Blot as described in Example 9 with the following modifications: 1 µl plasma, boiled with NuPAGE LDS sample buffer and sample reducing agent (Invitrogen) for 5 minutes, was used in the analysis; goat anti-human C2 was diluted to 1:2000 in 5% dry milk/TBST; and HRP-conjugated anti-goat secondary was diluted to 1:4000 in 5% dry milk/TBST. The results showed that *ex vivo* plasma from cynomolgus monkeys dosed with bolus IV injection of 1 or 3 mg/kg CB252 demonstrated partial cleavage of C2 at 3 mg/kg only. Plasma from monkeys treated with 1 mg/kg CB252 had no discernable C2 cleavage. Plasma collected from monkeys treated with 3 mg/kg CB252, there was a significant C2 cleavage observed for all three animals for which plasma samples were available. The average extent of degradation of C2 as determined by densitometry of C2 Western blots was 60% degraded at 5 minutes, 50% degraded at 30 minutes, and 40% degraded at 60 minutes. The percent inhibition of complement as assessed by C2 cleavage in plasma from all animals treated with 3 mg/kg CB252 are summarized in Table 27 below.

Table 27: CB252 Ex Vivo Complement Inhibition: C2 cleavage			
	Animal		
Time point	2	4	5
5 minutes	62%	55%	65%
30 minutes	55%	45%	50%
60 minutes	50%	37%	38%

2. C3b deposition

C3b deposition in the plasma samples was assessed by ELISA as described in Example 21. In the C3b deposition assay no significant inhibition of complement was observed in plasma samples from monkeys administered with 1 mg/kg CB252 administered for any animal at any time point assayed. At the 3 mg/kg dose of CB252, at 10% plasma, C3b deposition was inhibited by an average of approximately 50% at the 5 minute time point, 30% at the 30 minute time point, and 15% at 60 minutes. The level of inhibition by CB252 was observed to be greater when measured in 1% plasma. For the 3 mg/kg dose of CB252, at 1% plasma, C3b deposition was inhibited by an average of approximately 70% at 5 minutes, 55% at 30 minutes, and 50% at 60 minutes. The percent inhibition of complement as assessed by C3b deposition in plasma from all animals treated with 3 mg/kg CB252 are summarized in Table 28 below.

Table 28: CB252 Ex Vivo Complement Inhibition: C3b deposition						
	10% plasma			1% plasma		
	Animal			Animal		
Time point	2	4	5	2	4	5
5 minutes	52%	45%	50%	50%	74%	77%
30 minutes	37%	38%	13%	25%	60%	40%
60 minutes	40%	10%	3%	82%	16%	78%

3. Hemolysis

Hemolysis was assessed in the sensitized chicken red blood cell (RBC) hemolysis assay as described in Example 19. The results showed that plasma from monkeys treated with 1 mg/kg dose of CB252 exhibited no observable effect on hemolysis of sensitized chicken RBC for any animal at any time point assayed. Plasma samples from monkeys treated with 3 mg/kg CB252 showed significant inhibition of hemolysis at the various time points assayed, and inhibition was observed at 1%, 2.5% and 10% plasma. In 10% plasma, plasma from monkeys treated with 3 mg/kg CB252 showed an average of 80% inhibition of hemolysis at 5 minutes, 45% inhibition at 30 minutes, and 25% inhibition at 60 minutes. In 2.5% plasma, plasma from monkeys treated with 3 mg/kg CB252 showed an average of 92% inhibition of hemolysis at 5 minutes, 80% inhibition at 30 minutes, and 65% inhibition at 60 minutes. In 1% plasma, plasma from monkeys treated with 3 mg/kg CB252 showed an average of 99% inhibition of hemolysis at 5 minutes, 98% inhibition at 30 minutes, and 90% inhibition at 60 minutes. The percent inhibition of complement as assessed by hemolysis of chicken RBCs by plasma from all animals treated with 3 mg/kg CB252 are summarized in Table 29 below.

Table 29: CB252 Ex Vivo Complement Inhibition: Hemolysis

	10% Plasma			2.5% Plasma			1 % Plasma		
	Animals			Animals			Animals		
Time point (minutes)	2	4	5	2	4	5	2	4	5
5	55%	90%	80%	90%	95%	91%	96%	95%	97%
30	43%	65%	30%	85%	91%	62%	96%	95%	91%
60	ND	40%	10%	98%	78%	21%	96%	91%	79%

ND: not determined

In summary, cynomolgus plasma from monkeys treated with a single bolus intravenous injection of 1 mg/kg CB252 did not show significant inhibition of

complement as measured by C2 degradation, C3b deposition ELISA, or hemolysis of sensitized chicken red blood cells. Cynomolgus plasma from monkeys treated with a single bolus intravenous injection of 3 mg/kg CB252 did show significant inhibition of all ex vivo complement assays at the 5 minute and 30 minute time points. At the least stringent assay levels, 1% plasma in C3b deposition ELISA and 1% hemolysis, significant inhibition persists to the 60 minute time point.

B. Pharmacodynamic Efficacy of CB252 compared to other MT-SP1 mutants in Cynomolgus

Monkeys were injected intravenously with a bolus of CB252 or CB377 at 1 mg/kg and 3 mg/kg protease. Plasma was collected at various time points after injection (where t=0 is pre-injection; *i.e.* 0, 5, 30, and 60 minutes) and analyzed for complement activity by assaying for C2 cleavage by Western Blot as set forth in Example 9 and for hemolysis using the Cynomolgus hemolysis protocol as set forth in Example 19 using either 1%, 2.5%or 10% monkey plasma.

The results showed increased cleavage of C2 in plasma from CB252 and CB377 treated monkeys after treatment with 3 mg/kg protease but not after treatment with 1 mg/kg protease. Plasma collected from monkeys treated with 3 mg/kg CB252 and CB377 protease showed a time-dependent cleavage of C2, with greatest C2 cleavage occurring in plasma collected from monkeys at 5 minutes after protease treatment and decreased cleavage occurring at increased timepoints. The results also showed that a greater cleavage of C2 occurred in plasma collected form CB252 treated monkeys as compared to CB377 treated monkeys at all time points tested.

The results of the hemolysis experiment correlated with the C2 cleavage results since there was no observed difference in hemolysis induced by either 2.5% plasma or 10% plasma from monkeys treated with 1 mg/kg CB252 or CB377 protease at any of the collected time points as compared to hemolysis induced by plasma from monkeys not treated with protease (i.e. t=0). The results also showed that the hemolysis observed using either 2.5% or 10% plasma from monkeys treated with 3 mg/kg CB252 or CB377 was similar. Under both assay conditions, plasma from monkeys treated with 3 mg/kg CB377 showed only a slight decrease in hemolysis of erythrocytes as compared to plasma from t=0. The fraction of hemolysis at t=0 was set at 1.0 and the fraction hemolysis observed from plasma from CB377 treated

monkeys was about 0.7 for all time points tested. CB252 was markedly more potent than CB377 in this experiment. Plasma from monkeys treated with 3 mg/kg CB252 collected 5 minutes after injection induced no detectable hemolysis of erythrocytes with an observed fraction hemolysis of at or close to 0. The effects of CB252 on hemolysis was time-dependent since the fraction hemolysis induced from plasma from monkeys treated with 3 mg/kg CB252 increased to about 0.4 and about 0.7 in plasma collected 30 minutes and 60 minutes, respectively, from CB252 treated monkeys.

In another experiment, the pharmacodynamic efficacy of proteases CB238, CB252, and CB377 was compared upon administration to cynomolgus. Monkeys were injected intravenously with a bolus of CB238, CB252 or CB377 at the maximum tolerated dose (MTD) for each protease (*i.e.* 2 mg/kg, 3 mg/kg, and 3 mg/kg, respectively). Plasma was collected at various time points after injection (where t=0 is pre-injection; *i.e.* 0, 5, 30, and 60 minutes) and analyzed for complement activity by assaying for the ability to support hemolysis of chicken red blood cells using the Cynomolgus hemolysis protocol as set forth in Example 19 using either 2.5% or 10% monkey plasma. The % inhibition of hemolysis was determined as compared to hemolysis induced by 2.5 % or 10% plasma collected from t=0 monkeys. The results are summarized in Table 30 below.

Table 30: Cynomolgus Pharmacodynamics

Protease	Monkey MTD (mg/kg)	% inhib hemol (2.5% plasma) @ 5 min	% inhib hemol (2.5% plasma) @ 30 min	% inhib hemol (10% plasma) @ 5 min	% inhib hemol (10% plasma) @ 30 min
CB238	2	24	15	20	11
CB252	3	92	79	75	46
CB377	3	18	8	14	7

EXAMPLE 25
Examination of the Complement-Mediated Cardiovascular Effects of Proteases Ex Vivo in Rabbit Hearts

The effects of proteases on complement-mediated injury was assessed ex vivo using the Langendorff Assay to examine cardiac damage in rabbit hearts. Studies on

the isolated heart allows for simultaneous observations of a compound's hemodynamic, electrocardiographic, and electrophysiologic effects. New Zealand White rabbits were used in this study because the amino acid sequence of the rabbit I_{Kr} channel shares 99% homology with the human I_{Kr} channel sequence (Wymore *et al.* (1997) *Circ Res.*, 80: 261-268). The rabbit has been used extensively for cardiovascular studies and is an appropriate species to model potential effects on the human heart, since rabbit cardiac action potentials (similar to human cardiac action potentials) appear to be strongly driven by I_{Kr} (Weirich *et al.* (1998) *Basic Res Cardiol.*, 93:125-132; Carmeliet *et al.* (1992) *J Pharmacol Exp Ther.*, 262:809-817). Also, the interaction between human plasma and rabbit heart tissue has been previously characterized and has been shown to be primarily complement mediated (Kilgore *et al.* (1998) *J Pharmacol Exp. Ther.*, 285: 987-94). For example, contact of human plasma and the foreign surface of the rabbit heart activates complement, which then mediates damage to the myocardium ultimately resulting in asystole. Therefore, this model is appropriate to determine the efficacy of complement inhibitors, such as proteases or modified proteases that target one or more complement components.

A. Experimental Design and Methods

Rabbits were euthanized via stunning followed by cardiectomy. Hearts were rapidly removed, mounted on a Langendorff apparatus, and perfused with modified, oxygenated, Krebs-Henseleit buffer (37° C; Krebs-Henseleit buffer: 118.1 mM NaCl, 4.7 mM KCl, 1.17 mM $MgSO_4$, 1.18 mM KH_2PO_4, 11.1 mM d-glucose, 2.5 mM $CaCl_2$, 24.8 mM $NaHCO_3$, and 2.0 mM pyruvate; modified with the addition of 2.5g of bovine serum albumin/1000 ml of perfusion medium; and oxygenated via pressurized oxygen/carbon dioxide (95%/5%)). A ventricular drain and fluid-filled latex balloon was secured in the left ventricle with a purse string suture at the atrial appendage. A pulmonary artery drain was secured. Hearts were paced via pacing electrodes placed onto the right atrium. Hearts were deemed acceptable for the study if they exhibited acceptable hemodynamic parameters (*e.g.*, dP/dT > 1000 mm Hg/sec) throughout the equilibration period.

The protease test compound (at a final concentration of 1 μM) was incubated with incubation media (containing human plasma diluted to 50% in perfusion buffer;

i.e. 12 ml human serum diluted into 12 ml perfusion medium) for 1 hour at 37° C. Following the incubation, the test compound mixture was added to the experimental perfusion medium, recirculating, to give a final serum concentration of about 4- 6 % in 300 ml total volume. Isolated rabbit hearts that were previously equilibrated with perfusion medium for 10-15 minutes followed by collection of baseline measurements for 10 minutes, were exposed to perfusion medium containing the incubated test compound mixture for approximately 1 hour with measurements collected continuously as described below. The experiment was terminated if irreversible ventricular fibrillation occurred. Ventricular fibrillation was deemed irreversible if the heart did not spontaneously revert within 90 seconds of initiation. After exposure to the test compounds, the hearts were fixed in O.C.T., frozen on dry ice, and then stored in a freezer set at -80° C for immunohistochemistry evaluation.

1. **Hemodynamic Measurements**

The latex balloon in the left ventricle (LV) was expanded with water to achieve an LV end-diastolic pressure (LVEDP) of approximately 5 mmHg. The balloon was connected with tubing to a pressure transducer to measure LEPD, LV diastolic pressure (LVDP) and LV systolic pressure (LVSP). Coronary perfusion was measured with a pressure transducer connected to a side-arm port of the aortic cannula. Hemodynamic measurements were continuously monitored with the Notocord HEM (Kalamazoo, MI) v3.5 data capture system. Digital markers were used to indicate test compound exposure periods. LVDP was defined as the difference between LVEDP and LVSP. Both maximal rate of increase in LV pressure (+dP/dt) and minimal rate of decrease in LV pressure (-dP/dt) were measured, as the first derivative of the time from LVEDP to LVSP and LVSP to LVEDP, respectively. Coronary perfusion pressure (CPP) also was measured.

Hemodynamic measurements from the final minute of the equilibration period (0 min) and during the last minute of each 15 minute period (*i.e.* 15 min, 30 min, 45 min, 60 min) within the hour of the test compound exposure period were evaluated and used to determine effects of the test compound. Average values taken from five consecutive cardiac cycles uninterrupted by interference of ectopic beats were used for analysis of hemodynamic parameters. Values from each individual heart were

pooled to determine an average for each variable at individual concentrations. Average percent change of each variable between baseline and each concentration also was determined. The effect of each test compound on hemodynamic parameters was examined for statistical significance using repeated measures analysis of variance (ANOVA) followed by a post-hoc test for group comparisons when warranted. A value of $p < 0.05$ was considered statistically significant. Data was presented as mean ± SEM or percent change from baseline when appropriate.

2. Creatine Kinase Concentration Analysis

Approximately 2.0 ml of perfusion medium was collected just prior to the end of each 15 minute test period from the pulmonary artery drain. Prior to an early termination of the experiment (*e.g.*, due to ventricular fibrillation), a sample was taken for analysis. The samples were frozen on dry ice, and ten stored in a freezer set at -80° C for analysis.

B. Experimental Results

One micromolar of CB200, CB155, or CB42 was preincubated with human plasma diluted to 50% in perfusion medium for 1 hour at 37° C. The protease test compound mixture was then diluted to a final concentration of 6% plasma and perfused over isolated rabbit hearts to induce complement activation and the effects of the proteases on complement activation was determined based on hemodynamic measurements. Perfusion of hearts with heat-inactivated plasma was used as a negative control. Maximal rate of increase in LV pressure (+dP/dt) was determined at baseline (0 min), and 15, 30, 45, and 60 minutes after perfusion with the test compound proteases. The results show that plasma alone induced reduced rate of increase in LV pressure indicating damage to the mycocardium. The +dP/dt value was decreased about 5-fold from the baseline value and was similar between all time points tested. In contrast, plasma that was first heat-inactivated showed no change in the +dP/dt value as compared to that observed at baseline indicating no complement activation. Perfusion of rabbit hearts with protease test compounds protected the hearts from complement-mediated injury. Both CB42 and CB155 gave full protection of heart function as indicated by +dP/dt values comparable to baseline levels at all measured time points. CB200 (wildtype), however, only gave partial protection of

heart function in this model. At 15 minutes after perfusion with CB200, the heart function observed indicated almost complete protection with +dP/dt value comparable to baseline levels. By 30 minutes, CB200 showed little to no protection of heart function with greater than 3-fold decreased values of +dP/dt observed, approaching the levels observed by treatment of rabbit hearts with plasma alone. The rate of increase in LV pressure levels in rabbits perfused in the presence of CB200 remained low at 45 and 60 minutes indicating cardiac damage at these time points.

Example 26

Expression and Purification of Modified MT-SP1 CB238 in shake flasks

CB238 and related recombinant MT-SP1 mutants or wild-type MT-SP1 were cloned and expressed in E.coli as inclusion bodies as described in Example 1 and 2 above. The production of the MT-SP1 or mutants was adapted for laboratory scale by optimizing production of the MT-SP1 mutant CB238 by pooling up to about 44 X 1 L shake flasks for subsequent isolation of the inclusion body pellets for solubilization and refolding. Briefly, 1 µl of plasmid DNA (from DNA miniprep purification) was mixed with 50 µl of BL-21 cells. The cells were incubated the plasmid DNA on ice for 30 minutes, and then heat shocked at 42°C for 45 seconds. The cells were then incubated on ice for 2 minutes for recovery. 500 µl of LB (LB; Difco LB Broth Lennox, approximate formulation per liter: 10.0 g Tryptone, 10.0 g Yeast Extract, 5.0 g Sodium Chloride) was added to the cells, and the culture was incubated at 37°C with shaking for 1 hour. 50 µl of the cells was then plated out on agar plates containing 50 µg/ml carbenicillin for selection. The plate was incubated at 37°C for 16-18 hours.

25 ml of LB containing 50 µg/ml carbenicillin was inoculated from a single colony and grown until fully confluent. 0.5 ml of the seed culture was added to 800 ml of 2XYT containing 10 µg/ml of carbenicillin and grown overnight (~12-16 hours; approximately 44 flasks). The cells were harvested by centrifugation at 6,000 x g in a Sorvall rotor # SLC4000. The cell pellets were pooled and weighed. From 35.2 L of *E. coli* culture, 320 g of wet cell pellet was obtained. 600 ml of a buffer containing 50 mM Potassium Phosphate (KPO_4) pH 7.4 and 300 mM Sodium Chloride (NaCl) was added to the cell pellet. After the cells were completely resuspended, the batch was split into two and each part was sonicated in a glass vessel on ice. The sonicator

was set at 60% duty cycle, output level 8, for 4 minutes. The sonication procedure was repeated two times for each sample. The resulting sonicated sample was centrifuged at 16,900 x g for 20 minutes at 4° C. The supernatant was poured out and replaced with ~300 ml of fresh buffer containing 50 mM KPO_4 pH 7.4, 300 mM NaCl, and 0.5% lauryldimethylamine oxide (LDAO) volume/volume. The inclusion body was resuspended using a spatula and the solution was stirred until homogenous. The stirred sample was then centrifuged again and the supernatant decanted. The LDAO wash was performed a total of three times followed by three rounds of washing with buffer containing 50 mM KPO_4 pH 7.4, 300 mM NaCl that does not contain LDAO.

To the 70 g of purified wet inclusion body, 700 ml of denaturing buffer (6 M Guanidine HCl in 100 mM Tris pH 8.0, 20 mM dithiothreitol (DTT) was added, and the protein was solubilized. The sample was then centrifuged at 20,400 x g for 30 minutes at 22°C, and the supernatant was collected. The protein solution was then slowly dripped into 35 L of refolding solution (100 mM Tris pH 8.0, 150 mM NaCl, 1.5 M Arginine, 5 mM reduced glutathione, 0.05 mM oxidized glutathione) while vigorously stirring. The protein solution was left at 4°C for 72 hrs.

The resulting protein solution was concentrated by hollow filtration to ~1-2L then dialyzed into 16 L of buffer containing 50 mM Tris pH 8.0, 50 mM NaCl at 4°C overnight. The buffer was exchanged for fresh buffer the following morning, and the sample was dialyzed for an additional 8 hours. The protease sample was then removed from the dialysis tubing and incubated at room temperature until auto-activation of the protease occurred by cleavage of the proregion to release the mature enzyme. Activity was monitored as described in Example 3 above using a fluorogenic RQAR-AMC substrate and SDS-PAGE. Upon complete activation, the sample was then dialyzed into buffer containing 50 mM HEPES pH 6.5 at 4°C overnight.

The protein solution was then loaded onto a Source 15S column (Amersham) and eluted using a buffer gradient from 50 mM HEPES pH 6.5 to 50 mM HEPES pH 6.5 containing 0.15 M NaCl. Prior to all chromatography steps, each column is washed in reverse with 0.5 N NaOH then rinsed with water. The active fractions were

pooled. An equal volume of buffer containing 2 M $(NH_4)_2SO_4$ in 50 mM PO_4 pH 7.0 was added, and the resulting solution was loaded onto a Phenyl Sepharose HP column pre-equilibrated with buffer containing 50 mM PO_4 pH 7.0, 1 M $(NH_4)_2SO_4$. The active protein was eluted with a buffer gradient from 50 mM PO_4 pH 7.0, 1 M $(NH_4)_2SO_4$ to 50 mM PO_4 pH 7.0. The active fractions were pooled and buffer exchanged into 50 mM HEPES pH 6.5. The sample was then reloaded and purified on Source 15Q as in the first chromatography step. Active fractions were then pooled, buffer exchanged into PBS using a stirred cell, and concentrated to ~10 mg/ml. A sample was removed to measure protein concentration, A280. Benzamidine was then added to a final concentration of 20 mM to the remaining sample prior to filtration of the protein sample through a 0.2 uM syringe filter. The protein solution was frozen in liquid nitrogen and stored at -80°C. The final yield was ~800 mg of pure protein (~20 mg of protease/L of culture). The purified protein was assayed for specific activity, purity, and endotoxin levels as described in Example 3 above.

A similar strategy was employed for other MT-SP1 mutants or wildtype MT-SP1. The protocol is altered depending on the specific mutant. For the mutants that don't purify well over Phenyl Sepharose, Benzamidine Sepharose was used instead. For example, the MT-SP1 mutant CB450 is purified over a Benzamidine column.

Example 27

Assessment of Hemolysis and Plasma Activity by a Panel of MT-SP1 mutants

A panel of proteases were tested for their ability to support classical hemolysis or alternative hemolysis following preincubation with 20% plasma as described in Example 7, part A.1.b and Example 7, part B.1 above. In addition, the proteases were tested for Plasma Activity as described in Example 6. Table 31 depicts the fraction classical hemolysis at 200 nM, the fraction alternative hemolysis at 500 nM, and the IC50 for each protease for both Classical and Alternative hemolysis.

In addition, the percent protease unbound by alpha-2 macroglobulin (a2M) also was determined. Inactivation of a protease by alpha-2 macroglobulin traps the protease in a complex where it is still able to turn over small fluorescent substrates, but unable to access large protein substrates. This property of alpha-2 macroglobulin complicates the assessment of a proteases activity in plasma. To determine the actual

activity of the free, uncomplexed protease in plasma, a two step measurement is required. First, the sample's activity on fluorescent substrates is measured. Second, a macromolecular inhibitor is added to bind all of the free protease (ATIII or M84R ecotin), and the protease activity trapped (and hence protected from inhibition) in alpha-2 macroglobulin is measured. The percent unbound by alpha-2 macroglobulin activity is the percentage of the plasma residual activity that is inhibited by the addition of the ecotin. Briefly, in a 0.2 mL PCR tube, 1 µL 10X protease was mixed with 9 µL human plasma in citrate (Innovative Research). An uninhibited control also was prepeared containing 1 µL 10X protease mixed with 9 µL PBST. The mixtures were incubated for 5 minutes at 37°C. The samples were diluted 250 fold in PBST and stored on ice. Two 50 µL aliquots for each sample were transferred to an opaque assay plate (Costar #3694) containing 2 µL PBST or 2 µL 520 nM M84R ecotin. The plates were incubated 10 minutes at room temperature. Five microliters 0.4 mM Ac-RQAR-AMC substrate was added and the fluorescence was measured over time with a SpectraMax M5 spectrafluorometer (Molecular Devices) set to read every 20 seconds for 30 minutes at 30°C (Ex: 380 nm, EM: 450 nm, Cut-off: 435 nm). The percent unbound by alpha-2 macroglobulin was calculated with the following formula: (1-([(Protease in plasma/Protease in PBST)-(Protease in plasma+ecotin/Protease in PBST)]/(Protease in plasma/Protease in PBST)))*100. The results of % unbound alpha-2 macroglobulin for the panel of proteases tested is set forth in Table 31 below.

Table 31: Assessment of Hemolysis and Activity of a Panel of Proteases

CB#	Mutations	Classical 200nM Hemolysis	Alternative 500 nM Hemolysis	Classical IC_{50} Hemolysis (nM)	Alternative IC_{50} Hemolysis (nM)	Plasma Activity	% Unbound by a2M
CB421	I41T/Y146D/Q175D/K224F	0.714	478.90	0.271		0.585	84%
CB422	I41T/Y146E/Q175D/K224N	0.050	50.35	0.150	111.8	0.511	83%
CB450	I41T/I46D/G151L/K224F	0.255	269.14	0.223	262.4	0.287	
CB476	I41T/Y146D/Q175D/K224L	0.111	87.26	0.217	162.3	0.595	89%
CB477	I41T/Y146D/Q175D/K224R	0.016	53.43	0.140	116.2	0.346	67%
CB478	I41T/Y146D/Q175D/K224N	0.254	86.48	0.316	230.3	0.550	89%

CB480	I41T/Y146D/G151L/Q175D/K224F	0.272	131.01	0.367	268.1	0.670	88%
CB481	I41T/Y146D/G151L/Q175D/K224L	0.050	143.19	0.169	154.3	0.687	72%
CB482	I41T/Y146D/G151L/Q175D/K224R	0.042	57.39	0.255	296.2	0.306	10%
CB483	I41T/Y146D/G151L/Q175D/K224N	0.076	57.39	0.425	257.3	0.642	73%
CB484	I41T/Y146E/Q175D/K224F	0.235	67.21	0.365	268.5	0.649	94%
CB485	I41T/Y146E/Q175D/K224L	0.072	103.78	0.184	160.4	0.593	82%
CB486	I41T/Y146E/Q175D/K224R	0.014	43.36	0.128	125.4	0.326	44%
CB487	I41T/Y146E/G151L/Q175D/K224N	0.026	52.87	0.173	169.2	0.548	53%
CB488	I41T/Y146E/G151L/Q175D/K224F	0.086	72.61	0.195	179.3	0.658	85%
CB489	I41T/Y146E/G151L/Q175D/K224L	0.038	50.56	0.143	140.8	0.526	58%
CB490	I41T/Y146E/G151L/Q175D/K224R	0.031	52.63	0.125	193.8	0.288	0%

Example 28
Additional Mutants

Additional mutants are prepared as described herein. Such mutants include, but are not limited to, those set forth in Table 32 below.

Table 32: Additional Mutants	SEQ ID	SEQ ID
I41T/Y146D/G151L/K224N	681	696
Y146D/Q175D/K224N	682	697
I41T/Y146D/K224N	683	698
Y146D/G151L/K224N	684	699
Y146D/Q175R/K224N	685	700
Y146D/Q175K/K224N	686	701
Y146D/Q175H/K224N	687	702
I41T/Y146D/G151L/Q175K/K224F	688	703
I41T/Y146D/G151L/Q175R/K224F	689	704
I41T/Y146D/G151L/Q175H/K224F	690	705
I41T/Y146D/G151L/Q175Y/K224F	691	706
I41T/Y146D/G151L/Q175K/K224N	692	707
I41T/Y146D/G151L/Q175R/K224N	693	708
I41T/Y146D/G151L/Q175H/K224N	694	709
I41T/Y146D/G151L/Q175Y/K224N	695	710

CLAIMS:

1. A method of modulating complement activation, comprising contacting a non-complement protease with any one or more target substrates of a complement pathway, whereby a target substrate protein is cleaved such that complement activation in a pathway comprising the target substrate is altered.

2. The method of claim 1, wherein contacting the non-complement protease with any one or more target substrates of a complement pathway occurs *in vitro*.

3. The method of claim 1, wherein contacting the non-complement protease with any one or more target substrates of a complement pathway occurs *in vivo*.

4. The method of claim 1, wherein contacting the non-complement protease with any one or more target substrates of a complement pathway occurs *ex vivo*.

5. The method of any one of claims 1-4, wherein complement activation is inhibited.

6. The method of any one of claims 1-4, wherein complement activation is increased.

7. The method of any of claims 1-6, wherein the complement pathway is selected from among one or more of the classical, alternative and lectin pathways of complement.

8. The method of any of claims 1-7, wherein the target substrate is any one or more of C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a, C2b, C2a, C3b, C3a, Ba and Bb.

9. The method of any of claims 1-8, wherein the target substrate comprises a sequence of amino acids set forth in any one of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, and 344, or comprises a fragment thereof that exhibits a complement activity.

10. The method of any of claims 1-7, wherein the target substrate is a ficolin.

11. The method of claim 10, wherein the target substrate comprises a sequence of amino acids set forth in any of SEQ ID NOS: 660-662.

12. The method of any of claims 1-11, wherein the non-complement protease comprises modifications at any one or more amino acid residues compared to an unmodified or scaffold protease, wherein the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate.

13. The method of claim 12, wherein the unmodified or scaffold protease is any one of a serine protease, a cysteine protease, an aspartic protease, a threonine protease, or a metallo-protease.

14. The method of claim 13, wherein the scaffold protease is selected from among granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof.

15. The method of claim 14, wherein the scaffold protease comprises a sequence of amino acids set forth in any one of SEQ ID NOS: 2, 4, 8, 77, 79, 83, 85, 87, 89, 93, 99, 117, 119, 121, 123, 132, 134, 138, 142, 144, 146, 148, 162, 166, 168, 170, 172, 174, 176, 178, 180, 182, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 218, 220, 222, 224, 226, 238, 248, 250, 260, 262, 280, 282, 373, 375, 377, 379, 381, 383, 385, 387, 547, 549, and 551 and catalytically active portions thereof.

16. The method of claim 14, wherein the scaffold protease is an MT-SP1 protease.

17. The method of claim 16, wherein an MT-SP1 protease or a catalytically active portion thereof comprises a sequence of amino acids set forth in SEQ ID NO: 2 or 10, or is an allelic or species variant thereof.

18. The method of any of claims 16 or 17, wherein the target substrate is C2 or C3.

19. The method of claim 16, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 224 and/or position 146, based on chymotrypsin numbering.

20. The method of claim 18, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 224 and/or position 146, based on chymotrypsin numbering.

21. The method of claim 16, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 151, based on chymotrypsin numbering.

22. The method of claim 18, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 151, based on chymotrypsin numbering.

23. The method of claim 21 or claim 22, wherein the modification in an MT-SP1 protease or catalytically active portion thereof correspond to a protease having a modification selected from among I41T/Y146D/G151L/K224F, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, AND I41T/Y146D/G151L/Q175D/K224N, I41T/Y146D/G151L/K224N, Y146D/G151L/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N based on chymotrypsin numbering.

24. The method of claims 16 or 17, wherein the modifications in the MT-SP1 protease or a catalytically active portion thereof are in any one or more amino acids that contribute to extended substrate specificity or secondary sites of interaction.

25. The method of claim 24, wherein the modifications in an MT-SP1 protease or a catalytically active portion thereof correspond to any one or more of

amino acid positions 97, 146, 192, and 224 of an MT-SP1 protease, based on chymotrypsin numbering.

26. The method of claim 25, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to any one or more of amino acids F97, Y146, Q192, and K224 of the MT-SP1 protease, based on chymotrypsin numbering.

27. The method of claim 26, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from any one or more of F97D, F97E, F97A, F97W, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Q192R, Q192V, K224A, and K224F.

28. The method of claim 16 or 17, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof corresponds to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710.

29. The method of claim 27, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are Y146D/K224F or Y146E.

30. The method of claim 28, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in SEQ ID NOS: 596 or 650.

31. The method of claim 16 or claim 17, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from among F97N, F97D, F97E, F99Y, F99V, F99W, D217A, D217V, F97A, F97W, F99A, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, W215F, W215Y, Q192V, Q192R, Q192F, K224A, K224F, M180E, Y146D/K224F, D96A, Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E,

Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, I41T/Y146E/Q175D/K224L, I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering.

32. The method of claim 31, wherein the MT-SP1 protease cleaves a target substrate at a substrate recognition site.

33. The method of claim 32, wherein the target substrate is C2 or C3.

34. The method of claim 33, wherein the target substrate is C2 and the substrate recognition site includes a sequence of amino acids of SLGR (SEQ ID NO:392).

35. The method of any of claims 1-24, wherein the non-complement protease cleaves a substrate recognition site of a target substrate.

36. The method of claim 35, wherein the non-complement protease cleaves a Factor I substrate recognition site.

37. A method for treating a subject with a complement-mediated disorder, comprising administering a non-complement protease, whereby the non-complement protease cleaves any one or more target substrates of a complement pathway such that complement activation in a pathway comprising the target substrate is altered.

38. The method of claim 37, wherein complement activation is inhibited.

39. The method of claim 38, wherein the inhibition of complement activation leads to a reduction of inflammatory symptoms associated with a complement-mediated disorder selected from among an inflammatory disorder, a neurodegenerative disorder and a cardiovascular disorder.

40. The method of claim 39, wherein the complement-mediated disorder is selected from among sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), and Ischemia-reperfusion injury.

41. The method of claim 39, wherein the complement-mediated disorder is Guillan-Barre syndrome.

42. The method claim 40, wherein the ischemia-reperfusion injury is caused by an event or treatment selected from among myocardial infarct (MI), stroke, angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.

43. The method of any of claims 37-42, wherein the complement-mediated disorder results from a treatment of a subject.

44. The method of claim 43, wherein administering a non-complement protease is effected prior to treatment of a subject.

45. The method of claim 37-44, wherein administering a non-complement protease is effected by contacting a body fluid or tissue sample *in vitro*, *ex vivo*, or *in vivo* with a non-complement protease.

46. The method of claim 43, wherein the treatment results in complement-mediated ischemia-reperfusion injury.

47. The method of claim 46, wherein the treatment is angioplasty or coronary artery bypass graft.

48. The method of any of claims 37-47, wherein the complement pathway is one or more of the classical, alternative and lectin pathways.

49. The method of any of claims 37-48, wherein the target substrate is any one or more of C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a, C2b, C2a, C3b, C3a, Ba and Bb.

50. The method of any of claims 37-49, wherein the target substrate comprises a sequence of amino acids set forth in any one of SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, or 344, or comprises a fragment thereof that exhibits a complement activity.

51. The method of any of claims 37-48, wherein the target substrate is ficolin.

52. The method of claim 49, wherein the non-complement protease comprises modifications at any one or more amino acid residues compared to an unmodified or scaffold protease, wherein the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate.

53. The method of claim 52, wherein the unmodified or scaffold protease is any one of a serine protease, cysteine protease, aspartic protease, threonine protease, or metallo-protease.

54. The method of claim 53, wherein the scaffold protease is is selected from among granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin, protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof.

55. The method of claim 54, wherein the scaffold protease comprises a sequence of amino acids as set forth in any one of SEQ ID NOS: 2, 4, 8, 77, 79, 83, 85, 87, 89, 93, 99, 117, 119, 121, 123, 132, 134, 138, 142, 144, 146, 148, 162, 166, 168, 170, 172, 174, 176, 178, 180, 182, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 218, 220, 222, 224, 226, 238, 248, 250, 260, 262, 280, 282, 373, 375, 377, 379, 381, 383, 385, 387, 547, 549, and 551 and catalytically active portions thereof.

56. The method of claim 54, wherein the scaffold protease is an MT-SP1 protease.

57. The method of claim 56, wherein an MT-SP1 protease or a catalytically active portion thereof comprises a sequence of amino acids set forth in SEQ ID NO: 2 or 10, or is an allelic or species variant thereof.

58. The method of any of claims 56 or 57, wherein the target substrate is C2 or C3.

59. The method of claim 56, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 224, based on chymotrypsin numbering.

60. The method of claim 58, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 224, based on chymotrypsin numbering.

61. The method of claim 56, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 151, based on chymotrypsin numbering.

62. The method of claim 58, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 151, based on chymotrypsin numbering.

63. The method of claim 61 or claim 62, wherein the modification in an MT-SP1 protease or catalytically active portion thereof is selected from among I41T/Y146D/G151L/K224F, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, AND I41T/Y146D/G151L/Q175D/K224N, I41T/Y146D/G151L/K224N, Y146D/G151L/K224N, I41T/Y146D/G151L/Q175K/K224F,

I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N based on chymotrypsin numbering.

64. The method of claims 56 or 57, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are in any one or more amino acids that contribute to extended substrate specificity or secondary sites of interaction.

65. The method of claim 64, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to any one or more of amino acid positions 97, 146, 192, and 224 of an MT-SP1 protease, based on chymotrypsin numbering.

66. The method of claim 65, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to any one or more of amino acids F97, Y146, Q192, and K224 of the MT-SP1 protease, based on chymotrypsin numbering.

67. The method of claim 66, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from any one or more of F97D, F97E, F97A, F97W, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, Q192R, Q192V, K224A, and K224F.

68. The method of claim 56 or 57, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof corresponds to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in any of SEQ ID NOS: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40-69, 404-418, 419-447, 524-533, 552-659, or 663-710.

69. The method of claim 67, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are Y146D/K224F or Y146E.

70. The method of claim 68, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in SEQ ID NO:596 or 650.

71. The method of claim 56 or claim 57, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from among

F97N, F97D, F97E, F99Y, F99V, F99W, D217A, D217V, F97A, F97W, F99A, Y146N, Y146D, Y146E, Y146A, Y146W, Y146R, W215F, W215Y, Q192V, Q192R, Q192F, K224A, K224F, M180E, Y146D/K224F, D96A, Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD, Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, I41T/Y146E/Q175D/K224L, I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering.

72. The method of claim 71, wherein the MT-SP1 protease cleaves a substrate recognition site of the target substrate.

73. The method of claim 72, wherein the target substrate is C2 or C3.

74. The method of claim 73, wherein the target substrate is C2 and the substrate recognition site includes a sequence of amino acids of SLGR (SEQ ID NO:392).

75. The method of any of claims 37-74, wherein the non-complement protease cleaves a substrate recognition site of the target substrate.

76. The method of claim 75, wherein the non-complement protease cleaves a Factor I substrate recognition site.

77. The method of any one of claims 37-76, wherein the non-complement protease or a catalytically active portion thereof is administered in combination with a second agent for treating a complement-mediated disorder.

78. The method of claim 77, wherein the second agent is an anti-inflammatory agent or an anticoagulant.

79. The method of claim 78, wherein the second agent is selected from among any one or more of a NSAID, antimetabolite, corticosteroid, analgesic, cytotoxic agent, pro-inflammatory cytokine inhibitor, anti-inflammatory cytokines, B cell targeting agents, compounds targeting T antigens, adhesion molecule blockers, chemokines receptor antagonists, kinase inhibitors, PPAR-γ ligands, complement inhibitors, heparin, warfarin, acenocoumarol, phenindione, EDTA, citrate, oxalate, argatroban, lepirudin, bivalirudin, and ximelagatran.

80. A combination, comprising:

(a) a non-complement protease that cleaves any one or more complement target substrates of a complement pathway such that complement activation in a pathway comprising the target substrate is altered; and

(b) a second agent or agents for treating a complement-mediated disorder.

81. The combination of claim 80, wherein the second agent or agents is an anti-inflammatory agent(s) or anticoagulant(s).

82. The combination of claim 81 wherein, the anti-inflammatory agent(s) is selected from among any one or more of a NSAID, antimetabolite, corticosteroid, analgesic, cytotoxic agent, pro-inflammatory cytokine inhibitor, anti-inflammatory cytokines, B cell targeting agents, compounds targeting T antigens, adhesion

molecule blockers, chemokines receptor antagonists, kinase inhibitors, PPAR-γ ligands, complement inhibitors, heparin, warfarin, acenocoumarol, phenindione, EDTA, citrate, oxalate, argatroban, lepirudin, bivalirudin, and ximelagatran.

83. The combination of any one of claims 80-82, wherein complement activation is inhibited.

84. A modified non-complement protease, comprising modifications in any one or more amino acids of a scaffold protease, wherein:

the modified amino acid residue(s) increases one or both of specificity for a target substrate or activity towards a target substrate, wherein the target substrate is a complement protein.

85. The modified non-complement protease of claim 84, wherein the target substrate is any one or more of C1q, C2, C3, iC3, C4, iC4, C5, C6, C7, C8, C9, MBL, Factor B, Factor D, Factor P, MASP-1, MASP-2, C1r, C1s, C4b, C4a, C2b, C2a, C3b, C3a, Ba, or Bb.

86. The modified non-complement protease of claims 84 or 85, wherein the target substrate comprises a sequence of amino acids set forth in any one SEQ ID NOS: 298, 299, 300, 302, 304, 305, 306, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 326, 328, 330, 332, 334, 335, 338, 340, and 344, or comprises a fragment thereof that exhibits a complement activity.

87. The modified non-complement protease of claim 84, wherein the target substrate is a ficolin.

88. The modified non-complement protease of claim 87, wherein the target substrate comprises a sequence of amino acids set forth in any of SEQ ID NOS:660-662.

89. The modified non-complement protease of claim 84, wherein the scaffold protease is selected from among a serine protease, cysteine protease, aspartic protease, threonine protease, and metallo-protease.

90. The modified non-complement protease of claim 89, wherein the scaffold protease is selected from among granzyme B, granzyme A, granzyme M, cathepsin G, MT-SP1, neutrophil elastase, chymase, alpha-tryptase, beta-tryptase I or II, chymotrypsin, collagenase, factor XII, factor XI, factor CII, factor X, thrombin,

protein C, u-plasminogen activator (u-PA), t-plasminogen activator (t-PA), plasmin, plasma kallikrein, chymotrypsin, trypsin, a cathepsin, papain, cruzain, a metalloprotease and allelic variations, isoforms and catalytically active portions thereof.

91. The modified non-complement protease of claim 90, wherein the scaffold protease comprises a sequence of amino acids as set forth in any one of SEQ ID NOS: 2, 4, 8, 77, 79, 83, 85, 87, 89, 93, 99, 117, 119, 121, 123, 132, 134, 138, 142, 144, 146, 148, 162, 166, 168, 170, 172, 174, 176, 178, 180, 182, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 218, 220, 222, 224, 226, 238, 248, 250, 260, 262, 280, 282, 373, 375, 377, 379, 381, 383, 385, 387, 547, 549, and 551 and catalytically active portions thereof.

92. The modified non-complement protease of claim 90, wherein the scaffold protease is an MT-SP1 protease.

93. The modified non-complement protease of claim 92, wherein the MT-SP1 protease or a catalytically active portion thereof comprises a sequence of amino acids set forth in SEQ ID NO: 2 or 10.

94. The modified non-complement protease of claims 92 or 93, wherein the target substrate is C2 or C3.

95. The modified non-complement protease of claim 92, comprising at least two or more modifications, wherein one modification is at position 146 and the second modification is at position 224, based on chymotrypsin numbering, provided that:

(i) where the protease includes only two modifications, the protease does not include Y146D and K224F as the two modification; and

(ii) where the protease contains three modifications, the protease does not include F99V or I or L or T with Y146D and K224F.

96. The modified non-complement protease of claim 94, comprising at least two or more modifications, wherein one modification is a position 146 and the second is at position 224, based on chymotrypsin numbering, provided that:

(i) where the protease includes only two modifications, the protease does not include Y146D and K224F as the two modification; and

(ii) where the protease contains three modifications, the protease does not include F99V or I or L or T with Y146D and K224F.

97. The modified non-complement protease of claim 92, comprising at least one modification at position 151, based on chymotrypsin numbering.

98. The modified non-complement protease of claim 94, comprising at least one modification at position 151, based on chymotrypsin numbering.

99. The modified non-complement protease of claim 97 or claim 98, wherein modification(s) in an MT-SP1 or catalytically active portion are selected from among I41T/Y146D/G151L/K224F, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, AND I41T/Y146D/G151L/Q175D/K224N, I41T/Y146D/G151L/K224N, Y146D/G151L/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N based on chymotrypsin numbering.

100. The modified non-complement protease of claim 99, wherein modification(s) in an MT-SP1 or catalytically active portion correspond to modification of I41T/I46D/G151L/K224F, based on chymotrypsin numbering.

101. The modified non-complement protease of claim 92, wherein modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from any one or more of D96A, D96V, D96F, D96F, D96S, D96T, F99S, F99G, Q174H, Q174A, Q174V, Q174F, Q174R, Q174K, Q174L, Q174Y, Q192L, Q192I, Q192E, Q192K, Q192Y, D217Q, D217N, D217H, K224A, based on chymotrypsin numbering.

102. The modified non-complement protease of claim 92, wherein modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from among Y146E/K224N, I41T/Y146E/Q175D/K224R, I41T/Y146D/K224F, I41T/Y146E/Q175D/K224N, I41T/Y146E/G151L/Q175D/K224L, Y146E/ Q221aE/K224F, I41T/ Y146E/ G151L/Q175D/K224R, I41T/Y146E/G151L/Q175D/K224N, Q221aD,

Y146E/K224R, Y146E/ Q175D/ K224N, Y146D/K224R, I41T/Y146E/G151L/Q175D/K224F, Y146E/Q175D/K224R, Y146E/L224L, G147E, Y146D/Q175D/K224R, Y146D/Q175L/K224L, Y146D/Q175L/K224L, Y146D/Q175W/K224L, Y146D/K224L, Y146E/Q221aE/K224R, Y146E/ K224A, Y146D/Q175H/K224L, Y146D/Q175Y/K224L, Y146E/K224Y, Y146D/Q175F/K224L, Y146D/Q175F/K225L, Y146D/Q221aL/K224S, I41E/Y146D/K224L, Y146D/D217F/K224L, Y146D/D217F/K224L, H143V/Y146D/K224F, Y146E/K224F, Y146A/K224F, Y146E/K224T, I41T/Y146E/K224L, I41F/Y146D/K224F, I41L/Y146D/K224F, I41T/Y146D/G151L/K224F, I41A/Y146D/K224F, I41E/Y146D/K224F, I41D/Y146D/K224L, I41D/Y146D/K224F, Y146N/K224F, I41T/Y146D/Q175D/K224F, Q192F/K224F, Y146D/Q192A/K224F, Q192V/K224F, I41T/Y146D/Q175D/K224L, I41T/Y146D/Q175D/K224R, I41T/Y146D/Q175D/K224N, I41T/Y146D/G151L/Q175D/K224F, I41T/Y146D/G151L/Q175D/K224L, I41T/Y146D/G151L/Q175D/K224R, I41T/Y146D/G151L/Q175D/K224N, I41T/Y146E/Q175D/K224F, and I41T/Y146E/Q175D/K224L, , I41T/Y146D/G151L/K224N, Y146D/Q175D/K224N, Y146D/Q175D/K224N, Y146D/G151L/K224N, Y146D/Q175R/K224N, Y146D/Q175K/K224N, Y146D/Q175H/K224N, I41T/Y146D/G151L/Q175K/K224F, I41T/Y146D/G151L/Q175R/K224F, I41T/Y146D/G151L/Q175H/K224F, I41T/Y146D/G151L/Q175Y/K224F, I41T/Y146D/G151L/Q175K/K224N, I41T/Y146D/G151L/Q175R/K224N, I41T/Y146D/G151L/Q175H/K224N, and I41T/Y146D/G151L/Q175Y/K224N, based on chymotrypsin numbering.

103. The modified non-complement protease of claim 92, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof correspond to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in any one of SEQ ID NOS: 41-51, 56, 57, 60-64, 67, 69, 419-429, 431, 434, 435, 438-442, 445, 524, 525, 527-530, 532, 533, 552-659, or 663-710.

104. The modified non-complement protease of claim 92, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof

correspond to a modified MT-SP1 polypeptide having a sequence of amino acids as set forth in any one of SEQ ID NOS: 596 or 650.

105. The modified non-complement protease of claim 103, wherein the MT-SP1 protease cleaves a substrate recognition site of the target substrate.

106. The modified non-complement protease of claim 105, wherein the target substrate is C2 or C3.

107. The modified non-complement protease of claim 106, wherein the target substrate is C2 and the substrate recognition site includes a sequence of amino acids of SLGR (SEQ ID NO:392).

108. A pharmaceutical composition, comprising a modified non-complement protease of any of claims 84-107, 131, and 130.

109. A combination, comprising:

(a) a pharmaceutical composition of claim 108; and

(b) a second agent or agents for treating a complement-mediated disorder.

110. The pharmaceutical composition of claim 108, further comprising a pharmaceutically acceptable excipient.

111. The pharmaceutical composition of 110, wherein the pharmaceutical composition is formulated for systemic, oral, nasal, pulmonary, local, or topical administration.

112. A kit, comprising the pharmaceutical composition of any one of claims 108 or 109, a device for administration of the composition and, optionally, instructions for administration.

113. A nucleic acid molecule, comprising a sequence of nucleotides that encodes any one of the modified non-complement proteases of claims 84-107.

114. A vector, comprising the nucleic acid molecule of claim 113.

115. A cell, comprising the vector of claim 114.

116. A method of treatment, comprising administering to a subject a nucleic acid molecule of claim 113.

117. The method of treatment of claim 116, wherein the nucleic acid molecule is introduced into a vector for administration.

118. The method of treatment of claim 117, wherein the vector is an expression vector.

119. The method of treatment of claim 118, wherein the vector is episomal.

120. The method of treatment of claim 117 or 118, wherein the expression vector is selected from among an adenovirus vector, an adeno-associated virus vector, EBV, SV40, cytomegalovirus vector, vaccinia virus vector, herpesvirus vector, a retrovirus vector, a lentivirus vector, or an artificial chromosome.

121. The method of treatment of any of claims 117-120, wherein the nucleic acid is administered *in vivo* or *ex vivo*.

122. The method of treatment of claim 121, wherein *ex vivo* treatment comprises administering the nucleic acid into a cell *in vitro,* followed by administration of the cell into the subject.

123. The method of treatment of claim 122, wherein the cell is from a suitable donor or from the subject to be treated.

124. The method of treatment of claim 116-123, wherein the subject is a human.

125. A fusion protein, comprising a catalytically active portion of a protease of any of claims 84-107, 131, and 130 that is fused to a non-protease polypeptide.

126. The method of claim 16, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 41, based on chymotrypsin numbering.

127. The method of claim 18, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof are selected from a protease having a modification in position 41, based on chymotrypsin numbering.

128. The method of claim 56, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 41, based on chymotrypsin numbering.

129. The method of claim 58, wherein the modification(s) in an MT-SP1 protease or a catalytically active portion thereof comprises a modification in position 41, based on chymotrypsin numbering.

130. The modified non-complement protease of claim 92, comprising at least one modification at position 41, based on chymotrypsin numbering.

131. The modified non-complement protease of claim 94, comprising at least one modification at position 41, based on chymotrypsin numbering.

132. Use of a non-complement protease of any of claims 84-107, 131, and 130 for formulation of a medicament for the treatment of a complement-mediated disease or disorder.

133. Use of a non-complement protease protease of any of claims 84-107, 131, and 130 for treatment of a complement-mediated disease or disorder.

134. Use of a non-complement protease for formulation of a medicament for the treatment of a complement-mediated disease or disorder.

135. Use of a non-complement protease for treatment of a complement-mediated disease or disorder.

136. Use of any of claims 132-135, wherein the non-complement protease cleaves any one or more target substrates of a complement pathway such that complement activation in a pathway comprising the target substrate is altered.

137. Use of claim 136, wherein complement activation is inhibited.

138. Use of claim 137, wherein the inhibition of complement activation leads to a reduction of inflammatory symptoms associated with a complement-mediated disorder selected from among an inflammatory disorder, a neurodegenerative disorder and a cardiovascular disorder.

139. Use of claim 138, wherein the complement-mediated disorder is selected from among sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), and Ischemia-reperfusion injury.

140. Use of claim 138, wherein the complement-mediated disorder is Guillan-Barre syndrome.

141. Use of claim 139, wherein the ischemia-reperfusion injury is caused by an event or treatment selected from among myocardial infarct (MI), stroke,

angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.

142. Use of any of claims 132-141, wherein the complement-mediated disorder results from a treatment of a subject.

143. The method of claim 142, wherein the treatment results in complement-mediated ischemia-reperfusion injury.

144. The method of claim 143, wherein the treatment is angioplasty or coronary artery bypass graft.

SEQUENCE LISTING

<110> Catalyst Biosciences, Inc.
Ed Madison
Jack Nguyen
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Christopher Thanos

<120> Modified Proteases That Inhibit Complement Activation

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    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
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Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
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Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
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Met Lys Leu Leu Leu Leu Leu Leu Ser Phe Ser Leu Ala Pro Lys Thr
 1               5                  10                  15
Glu Ala Gly Glu Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg
            20                  25                  30
Pro Tyr Met Ala Tyr Leu Gln Ile Met Asp Glu Tyr Ser Gly Ser Lys
        35                  40                  45
Lys Cys Gly Gly Phe Leu Ile Arg Glu Asp Phe Val Leu Thr Ala Ala
    50                  55                  60
His Cys Ser Gly Ser Lys Ile Asn Val Thr Leu Gly Ala His Asn Ile
65                  70                  75                  80
Lys Glu Gln Glu Lys Met Gln Gln Ile Ile Pro Val Val Lys Ile Ile
                85                  90                  95
Pro His Pro Ala Tyr Asn Ser Lys Thr Ile Ser Asn Asp Ile Met Leu
            100                 105                 110
Leu Lys Leu Lys Ser Lys Ala Lys Arg Ser Ser Ala Val Lys Pro Leu
        115                 120                 125
Asn Leu Pro Arg Arg Asn Val Lys Val Lys Pro Gly Asp Val Cys Tyr
    130                 135                 140
Val Ala Gly Trp Gly Lys Leu Gly Pro Met Gly Lys Tyr Ser Asp Thr
145                 150                 155                 160
Leu Gln Glu Val Glu Leu Thr Val Gln Glu Asp Gln Lys Cys Glu Ser
                165                 170                 175
Tyr Leu Lys Asn Tyr Phe Asp Lys Ala Asn Glu Ile Cys Ala Gly Asp
            180                 185                 190
Pro Lys Ile Lys Arg Ala Ser Phe Arg Gly Asp Ser Gly Gly Pro Leu
        195                 200                 205
Val Cys Lys Lys Val Ala Ala Gly Ile Val Ser Tyr Gly Gln Asn Asp
    210                 215                 220
Gly Ser Thr Pro Arg Ala Phe Thr Lys Val Ser Thr Phe Leu Ser Trp
225                 230                 235                 240
Ile Lys Lys Thr Met Lys Lys Ser
                245
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<210> 7
<211> 865
<212> DNA
<213> Homo sapiens

<400> 7

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ccctgccagc ggcaccatgg ctttcctctg gctcctctcc tgctgggccc tcctgggtac 60
caccttcggc tgcggggtcc ccgccatcca ccctgtgctc agcggcctgt ccaggatcgt 120
gaatggggag gacgccgtcc ccggctcctg gccctggcag gtgtccctgc aggacaaaac 180
cggcttccac ttctgcgggg gctccctcat cagcgaggac tgggtggtca ccgctgccca 240
ctgcggggtc aggacctccg acgtggtcgt ggctggggag tttgaccagg gctctgacga 300
ggagaacatc caggtcctga agatcgccaa ggtcttcaag aaccccaagt tcagcattct 360
gaccgtgaac aatgacatca ccctgctgaa gctggccaca cctgcccgct tctcccagac 420
agtgtccgcc gtgtgcctgc ccagcgccga cgacgacttc cccgcgggga cactgtgtgc 480
caccacaggc tggggcaaga ccaagtacaa cgccaacaag acccctgaca agctgcagca 540
ggcagccctg cccctcctgt ccaatgccga atgcaagaag tcctggggca ggaggatcac 600
cgacgtgatg atctgtgccg gggccagtgg cgtctcctcc tgcatgggcg actctggcgg 660
tcccctggtc tgccaaaagg atggagcctg gaccctggtg ggcattgtgt cctggggcag 720
cgacacctgc tccacctcca gccctggcgt gtacgcccgt gtcaccaagc tcataccttg 780
ggtgcagaag atcctggctg ccaactgagc ccgcggctcc ctccgaccct gctccccaca 840
gagcctcagt aaacccatgg aacac                                       865
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<210> 8

<211> 263
<212> PRT
<213> Homo sapiens

<400> 8

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Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr
 1               5                  10                  15
Phe Gly Cys Gly Val Pro Ala Ile His Pro Val Leu Ser Gly Leu Ser
            20                  25                  30
Arg Ile Val Asn Gly Glu Asp Ala Val Pro Gly Ser Trp Pro Trp Gln
        35                  40                  45
Val Ser Leu Gln Asp Lys Thr Gly Phe His Phe Cys Gly Gly Ser Leu
    50                  55                  60
Ile Ser Glu Asp Trp Val Val Thr Ala Ala His Cys Gly Val Arg Thr
65                  70                  75                  80
Ser Asp Val Val Val Ala Gly Glu Phe Asp Gln Gly Ser Asp Glu Glu
                85                  90                  95
Asn Ile Gln Val Leu Lys Ile Ala Lys Val Phe Lys Asn Pro Lys Phe
            100                 105                 110
Ser Ile Leu Thr Val Asn Asn Asp Ile Thr Leu Leu Lys Leu Ala Thr
        115                 120                 125
Pro Ala Arg Phe Ser Gln Thr Val Ser Ala Val Cys Leu Pro Ser Ala
    130                 135                 140
Asp Asp Asp Phe Pro Ala Gly Thr Leu Cys Ala Thr Thr Gly Trp Gly
145                 150                 155                 160
Lys Thr Lys Tyr Asn Ala Asn Lys Thr Pro Asp Lys Leu Gln Gln Ala
                165                 170                 175
Ala Leu Pro Leu Leu Ser Asn Ala Glu Cys Lys Lys Ser Trp Gly Arg
            180                 185                 190
Arg Ile Thr Asp Val Met Ile Cys Ala Gly Ala Ser Gly Val Ser Ser
        195                 200                 205
Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Asp Gly Ala
    210                 215                 220
Trp Thr Leu Val Gly Ile Val Ser Trp Gly Ser Asp Thr Cys Ser Thr
225                 230                 235                 240
Ser Ser Pro Gly Val Tyr Ala Arg Val Thr Lys Leu Ile Pro Trp Val
                245                 250                 255
Gln Lys Ile Leu Ala Ala Asn
            260
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<210> 9
<211> 723
<212> DNA
<213> Homo sapiens

<400> 9

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gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacttcacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
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aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 10
<211> 241
<212> PRT
<213> Homo sapiens

<400> 10
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 11
<211> 723
<212> DNA
<213> Homo sapiens

<400> 11
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacttcacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
gacggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540

agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
ttcccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 12
<211> 241
<212> PRT
<213> Homo sapiens

<400> 12
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 13
<211> 723
<212> DNA
<213> Homo sapiens

<400> 13
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacttcacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420

tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg cgtcggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 14
<211> 241
<212> PRT
<213> Homo sapiens

<400> 14
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Val Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 15
<211> 723
<212> DNA
<213> Homo sapiens

<400> 15
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacgacacct tcgactatga catcgcgctg 300

ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 16
<211> 241
<212> PRT
<213> Homo sapiens

<400> 16
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Asp Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 17
<211> 723
<212> DNA
<213> Homo sapiens

<400> 17
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180

ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacgagacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 18
<211> 241
<212> PRT
<213> Homo sapiens

<400> 18

Val	Val	Gly	Gly	Thr	Asp	Ala	Asp	Glu	Gly	Glu	Trp	Pro	Trp	Gln	Val
1				5				10					15		
Ser	Leu	His	Ala	Leu	Gly	Gln	Gly	His	Ile	Cys	Gly	Ala	Ser	Leu	Ile
			20					25				30			
Ser	Pro	Asn	Trp	Leu	Val	Ser	Ala	Ala	His	Cys	Tyr	Ile	Asp	Asp	Arg
		35					40					45			
Gly	Phe	Arg	Tyr	Ser	Asp	Pro	Thr	Gln	Trp	Thr	Ala	Phe	Leu	Gly	Leu
	50					55					60				
His	Asp	Gln	Ser	Gln	Arg	Ser	Ala	Pro	Gly	Val	Gln	Glu	Arg	Arg	Leu
65					70					75					80
Lys	Arg	Ile	Ile	Ser	His	Pro	Phe	Phe	Asn	Asp	Glu	Thr	Phe	Asp	Tyr
				85					90					95	
Asp	Ile	Ala	Leu	Leu	Glu	Leu	Glu	Lys	Pro	Ala	Glu	Tyr	Ser	Ser	Met
			100					105					110		
Val	Arg	Pro	Ile	Cys	Leu	Pro	Asp	Ala	Ser	His	Val	Phe	Pro	Ala	Gly
		115					120					125			
Lys	Ala	Ile	Trp	Val	Thr	Gly	Trp	Gly	His	Thr	Gln	Tyr	Gly	Gly	Thr
	130					135					140				
Gly	Ala	Leu	Ile	Leu	Gln	Lys	Gly	Glu	Ile	Arg	Val	Ile	Asn	Gln	Thr
145					150					155					160
Thr	Cys	Glu	Asn	Leu	Leu	Pro	Gln	Gln	Ile	Thr	Pro	Arg	Met	Met	Cys
				165					170					175	
Val	Gly	Phe	Leu	Ser	Gly	Gly	Val	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly
			180					185					190		
Gly	Pro	Leu	Ser	Ser	Val	Glu	Ala	Asp	Gly	Arg	Ile	Phe	Gln	Ala	Gly
		195					200					205			
Val	Val	Ser	Trp	Gly	Asp	Gly	Cys	Ala	Gln	Arg	Asn	Lys	Pro	Gly	Val
	210					215					220				
Tyr	Thr	Arg	Leu	Pro	Leu	Phe	Arg	Asp	Trp	Ile	Lys	Glu	Asn	Thr	Gly
225					230					235					240
Val															

<210> 19
<211> 723
<212> DNA
<213> Homo sapiens

<400> 19
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60

ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gacgccacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 20
<211> 241
<212> PRT
<213> Homo spaiens

<400> 20
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Ala Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 21
<211> 723
<212> DNA
<213> Homo sapiens

<400> 21
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 22
<211> 241
<212> PRT
<213> Homo sapiens

<400> 22
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1   5   10   15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20   25   30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35   40   45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50   55   60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65   70   75   80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85   90   95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100   105   110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115   120   125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130   135   140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145   150   155   160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165   170   175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180   185   190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195   200   205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210   215   220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225   230   235   240
Val

<210> 23
<211> 723
<212> DNA

<213> Homo sapiens

<400> 23
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
aacggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 24
<211> 241
<212> PRT
<213> Homo sapiens

<400> 24
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1   5   10   15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20   25   30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35   40   45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50   55   60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65   70   75   80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85   90   95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100   105   110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115   120   125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asn Gly Gly Thr
    130   135   140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145   150   155   160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165   170   175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180   185   190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195   200   205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210   215   220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225   230   235   240
Val

<210> 25

<211> 723
<212> DNA
<213> Homo sapiens

<400> 25
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
gacggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 26
<211> 241
<212> PRT
<213> Homo sapiens

<400> 26
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1   5   10   15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20   25   30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35   40   45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50   55   60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65   70   75   80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85   90   95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100   105   110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115   120   125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130   135   140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145   150   155   160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165   170   175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180   185   190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195   200   205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210   215   220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225   230   235   240
Val

<210> 27
<211> 723
<212> DNA
<213> Homo sapiens

<400> 27
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
gagggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 28
<211> 241
<212> PRT
<213> Homo sapiens

<400> 28
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 29
<211> 723
<212> DNA
<213> Homo sapiens

<400> 29
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
gccggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 30
<211> 241
<212> PRT
<213> Homo sapiens

<400> 30
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1   5   10   15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20   25   30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35   40   45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50   55   60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65   70   75   80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85   90   95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100   105   110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115   120   125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Ala Gly Gly Thr
    130   135   140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145   150   155   160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165   170   175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180   185   190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195   200   205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210   215   220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly

225 230 235 240
Val

<210> 31
<211> 723
<212> DNA
<213> Homo sapiens

<400> 31
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tggggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 32
<211> 241
<212> PRT
<213> Homo sapiens

<400> 32
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Trp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val

```
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 33
<211> 723
<212> DNA
<213> Homo sapiens

<400> 33
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
aggggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 34
<211> 241
<212> PRT
<213> Homo sapiens

<400> 34
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Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Arg Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
```

```
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 35
<211> 723
<212> DNA
<213> Homo sapiens

<400> 35
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
aggggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccggggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 36
<211> 241
<212> PRT
<213> Homo sapiens

<400> 36
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Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Arg Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Arg Gly Asp Ser Gly
```

```
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 37
<211> 723
<212> DNA
<213> Homo sapiens

<400> 37
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
aggggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccggggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
gcgccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta   723

<210> 38
<211> 241
<212> PRT
<213> Homo sapiens

<400> 38
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Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Arg Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
```

```
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Arg Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Ala Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 39
<211> 723
<212> DNA
<213> Homo sapiens

<400> 39
gttgttgggg gcacggatgc ggatgagggc gagtggccct ggcaggtaag cctgcatgct 60
ctgggccagg gccacatctg cggtgcttcc ctcatctctc ccaactggct ggtctctgcc 120
gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
aagcgcatca tctcccaccc cttcttcaat gactggacct tcgactatga catcgcgctg 300
ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttcctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
aggggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gcagcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccggggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
ttcccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta   723

<210> 40
<211> 241
<212> PRT
<213> Homo sapiens

<400> 40
```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Trp Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Arg Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
```

```
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Arg Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 41
<211> 241
<212> PRT
<213> Homo sapiens

<400> 41

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro His Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 42
<211> 241
<212> PRT

<213> Homo sapiens

<400> 42

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Gln Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 43
<211> 241
<212> PRT
<213> Homo sapiens

<400> 43

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
```

```
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asn Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 44
<211> 241
<212> PRT
<213> Homo sapiens

<400> 44

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly His Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 45
<211> 241
<212> PRT
<213> Homo sapiens

<400> 45
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Ala Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 46
<211> 241
<212> PRT
<213> Homo sapiens

<400> 46
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Val Phe Thr Phe Asp Tyr

```
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 47
<211> 241
<212> PRT
<213> Homo sapiens

<400> 47

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Phe Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
```

225 230 235 240
Val

<210> 48
<211> 241
<212> PRT
<213> Homo sapiens

<400> 48
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Ser Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 49
<211> 241
<212> PRT
<213> Homo sapiens

<400> 49
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu

```
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Thr Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 50
<211> 241
<212> PRT
<213> Homo sapiens

<400> 50

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Leu Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
```

```
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 51
<211> 241
<212> PRT
<213> Homo sapiens

<400> 51

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Ile Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 52
<211> 241
<212> PRT
<213> Homo sapiens

<400> 52

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
```

```
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Phe Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 53
<211> 241
<212> PRT
<213> Homo sapiens

<400> 53

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Phe Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
```

```
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 54
<211> 241
<212> PRT
<213> Homo sapiens

<400> 54

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Ala Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 55
<211> 241
<212> PRT
<213> Homo sapiens

<400> 55
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Val Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 56
<211> 241
<212> PRT
<213> Homo sapiens

<400> 56
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Ser Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr

```
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 57
<211> 241
<212> PRT
<213> Homo sapiens

<400> 57

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Gly Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 58

<211> 241
<212> PRT
<213> Homo sapiens

<400> 58
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Phe Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 59
<211> 241
<212> PRT
<213> Homo sapiens

<400> 59
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met

```
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Tyr Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 60
<211> 241
<212> PRT
<213> Homo sapiens

<400> 60

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Ala Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 61
<211> 241
<212> PRT
<213> Homo sapiens

<400> 61
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Val Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 62
<211> 241
<212> PRT
<213> Homo sapiens

<400> 62
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu

65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Phe Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 63
<211> 241
<212> PRT
<213> Homo sapiens

<400> 63
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Arg Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val

```
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 64
<211> 241
<212> PRT
<213> Homo sapiens

<400> 64

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Lys Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 65
<211> 241
<212> PRT
<213> Homo sapiens

<400> 65

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
```

```
          35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
     50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Ala Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 66
<211> 241
<212> PRT
<213> Homo sapiens

<400> 66

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
```

```
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Val Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 67
<211> 241
<212> PRT
<213> Homo sapiens

<400> 67

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Glu Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 68
<211> 241
<212> PRT
<213> Homo sapiens

<400> 68

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
```

```
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Trp Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 69
<211> 241
<212> PRT
<213> Homo sapiens

<400> 69

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Tyr Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
```

```
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 70
<211> 1165
<212> DNA
<213> Homo sapiens

<400> 70

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gctgggagta gagggcagag ctcccacccc gccccgcccc cagggggcgc cccgggcccg 60
gcgcgagagg aggcagaggg ggcgtcaggc cgcgggagag gaggccatgg gcgcgcgcgg 120
ggcgctgctg ctggcgctgc tgctggctcg ggctggactc aggaagccgg agtcgcagga 180
ggcggcgccg ttatcaggac catgcggccg acgggtcatc acgtcgcgca tcgtgggtgg 240
agaggacgcc gaactcgggc gttggccgtg gcaggggagc ctgcgcctgt gggattccca 300
cgtatgcgga gtgagcctgc tcagccaccg ctgggcactc acggcggcgc actgctttga 360
aacctatagt gaccttagtg atccctccgg gtggatggtc cagtttggcc agctgacttc 420
catgccatcc ttctggagcc tgcaggccta ctacacccgt tacttcgtat cgaatatcta 480
tctgagccct cgctacctgg ggaattcacc ctatgacatt gccttggtga agctgtctgc 540
acctgtcacc tacactaaac acatccagcc catctgtctc caggcctcca catttgagtt 600
tgagaaccgg acagactgct gggtgactgg ctgggggtac atcaaagagg atgaggcact 660
gccatctccc cacaccctcc aggaagttca ggtcgccatc ataaacaact ctatgtgcaa 720
ccacctcttc ctcaagtaca gtttccgcaa ggacatcttt ggagacatgg tttgtgctgg 780
caatgcccaa ggcgggaagg atgcctgctt cggtgactca ggtggaccct tggcctgtaa 840
caagaatgga ctgtggtatc agattggagt cgtgagctgg ggagtgggct gtggtcggcc 900
caatcggccc ggtgtctaca ccaatatcag ccaccacttt gagtggatcc agaagctgat 960
ggcccagagt ggcatgtccc agccagaccc ctcctggccg ctactctttt tccctcttct 1020
ctgggctctc ccactcctgg ggccggtctg agcctacctg agcccatgca gcctggggcc 1080
actgccaagt caggccctgg ttctcttctg tcttgtttgg taataaacac attccagttg 1140
atgccttgca gggcattctt caaaa                                      1165
```

<210> 71
<211> 314
<212> PRT
<213> Homo sapiens

<400> 71

```
Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg Ala
 1               5                  10                  15
Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser Gly Pro
            20                  25                  30
Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly Glu Asp Ala
        35                  40                  45
Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg Leu Trp Asp Ser
    50                  55                  60
His Val Cys Gly Val Ser Leu Leu Ser His Arg Trp Ala Leu Thr Ala
65                  70                  75                  80
```

```
Ala His Cys Phe Glu Thr Tyr Ser Asp Leu Ser Asp Pro Ser Gly Trp
                85                  90                  95
Met Val Gln Phe Gly Gln Leu Thr Ser Met Pro Ser Phe Trp Ser Leu
            100                 105                 110
Gln Ala Tyr Tyr Thr Arg Tyr Phe Val Ser Asn Ile Tyr Leu Ser Pro
        115                 120                 125
Arg Tyr Leu Gly Asn Ser Pro Tyr Asp Ile Ala Leu Val Lys Leu Ser
    130                 135                 140
Ala Pro Val Thr Tyr Thr Lys His Ile Gln Pro Ile Cys Leu Gln Ala
145                 150                 155                 160
Ser Thr Phe Glu Phe Glu Asn Arg Thr Asp Cys Trp Val Thr Gly Trp
                165                 170                 175
Gly Tyr Ile Lys Glu Asp Glu Ala Leu Pro Ser Pro His Thr Leu Gln
            180                 185                 190
Glu Val Gln Val Ala Ile Ile Asn Asn Ser Met Cys Asn His Leu Phe
        195                 200                 205
Leu Lys Tyr Ser Phe Arg Lys Asp Ile Phe Gly Asp Met Val Cys Ala
    210                 215                 220
Gly Asn Ala Gln Gly Gly Lys Asp Ala Cys Phe Gly Asp Ser Gly Gly
225                 230                 235                 240
Pro Leu Ala Cys Asn Lys Asn Gly Leu Trp Tyr Gln Ile Gly Val Val
                245                 250                 255
Ser Trp Gly Val Gly Cys Gly Arg Pro Asn Arg Pro Gly Val Tyr Thr
            260                 265                 270
Asn Ile Ser His His Phe Glu Trp Ile Gln Lys Leu Met Ala Gln Ser
        275                 280                 285
Gly Met Ser Gln Pro Asp Pro Ser Trp Pro Leu Leu Phe Phe Pro Leu
    290                 295                 300
Leu Trp Ala Leu Pro Leu Leu Gly Pro Val
305                 310
```

<210> 72
<211> 1159
<212> DNA
<213> Homo sapiens

<400> 72

```
gctgggagta gagggcagag ctcccacccc gccccgcccc caggggcgc cccgggcccg 60
gcgcgagagg aggcagaggg ggcgtcaggc cgcgggagag gaggccatgg gcgcgcgcgg 120
ggcgctgctg ctggcgctgc tgctggctcg ggctggactc aggaagccgg agtcgcagga 180
ggcggcgccg ttatcaggac catgcggccg acgggtcatc acgtcgcgca tcgtgggtgg 240
agaggacgcc gaactcgggc gttggccgtg gcaggggagc ctgcgcctgt gggattccca 300
cgtatgcgga gtgagcctgc tcagccaccg ctgggcactc acggcggcgc actgctttga 360
aactgacctt agtgatccct ccgggtggat ggtccagttt ggccagctga cttccatgcc 420
atccttctgg agcctgcagg cctactacac ccgttacttc gtatcgaata tctatctgag 480
ccctcgctac ctggggaatt caccctatga cattgccttg gtgaagctgt ctgcacctgt 540
cacctacact aaacacatcc agcccatctg tctccaggcc tccacatttg agtttgagaa 600
ccggacagac tgctgggtga ctggctgggg gtacatcaaa gaggatgagg cactgccatc 660
tccccacacc ctccaggaag ttcaggtcgc catcataaac aactctatgt gcaaccacct 720
cttcctcaag tacagtttcc gcaaggacat ctttggagac atggtttgtg ctggcaatgc 780
ccaaggcggg aaggatgcct gcttcggtga ctcaggtgga cccttggcct gtaacaagaa 840
tggactgtgg tatcagattg gagtcgtgag ctggggagtg ggctgtggtc ggcccaatcg 900
gcccggtgtc tacaccaata tcagccacca ctttgagtgg atccagaagc tgatggccca 960
gagtggcatg tcccagccag acccctcctg gccgctactc tttttccctc ttctctgggc 1020
tctcccactc ctggggccgg tctgagccta cctgagccca tgcagcctgg ggccactgcc 1080
aagtcaggcc ctggttctct tctgtcttgt ttggtaataa acacattcca gttgatgcct 1140
tgcagggcat tcttcaaaa                                          1159
```

<210> 73
<211> 312
<212> PRT
<213> Homo sapiens

<400> 73

```
Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg Ala
 1               5                  10                  15
Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser Gly Pro
            20                  25                  30
Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly Glu Asp Ala
        35                  40                  45
Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg Leu Trp Asp Ser
    50                  55                  60
His Val Cys Gly Val Ser Leu Leu Ser His Arg Trp Ala Leu Thr Ala
65                  70                  75                  80
Ala His Cys Phe Glu Thr Asp Leu Ser Asp Pro Ser Gly Trp Met Val
                85                  90                  95
Gln Phe Gly Gln Leu Thr Ser Met Pro Ser Phe Trp Ser Leu Gln Ala
            100                 105                 110
Tyr Tyr Thr Arg Tyr Phe Val Ser Asn Ile Tyr Leu Ser Pro Arg Tyr
        115                 120                 125
Leu Gly Asn Ser Pro Tyr Asp Ile Ala Leu Val Lys Leu Ser Ala Pro
    130                 135                 140
Val Thr Tyr Thr Lys His Ile Gln Pro Ile Cys Leu Gln Ala Ser Thr
145                 150                 155                 160
Phe Glu Phe Glu Asn Arg Thr Asp Cys Trp Val Thr Gly Trp Gly Tyr
                165                 170                 175
Ile Lys Glu Asp Glu Ala Leu Pro Ser Pro His Thr Leu Gln Glu Val
            180                 185                 190
Gln Val Ala Ile Ile Asn Asn Ser Met Cys Asn His Leu Phe Leu Lys
        195                 200                 205
Tyr Ser Phe Arg Lys Asp Ile Phe Gly Asp Met Val Cys Ala Gly Asn
    210                 215                 220
Ala Gln Gly Gly Lys Asp Ala Cys Phe Gly Asp Ser Gly Gly Pro Leu
225                 230                 235                 240
Ala Cys Asn Lys Asn Gly Leu Trp Tyr Gln Ile Gly Val Val Ser Trp
                245                 250                 255
Gly Val Gly Cys Gly Arg Pro Asn Arg Pro Gly Val Tyr Thr Asn Ile
            260                 265                 270
Ser His His Phe Glu Trp Ile Gln Lys Leu Met Ala Gln Ser Gly Met
        275                 280                 285
Ser Gln Pro Asp Pro Ser Trp Pro Leu Leu Phe Phe Pro Leu Leu Trp
    290                 295                 300
Ala Leu Pro Leu Leu Gly Pro Val
305                 310
```

<210> 74
<211> 1135
<212> DNA
<213> Homo sapiens

<400> 74

```
gctgggagta gagggcagag ctcccacccc gccccgcccc caggggcgc cccgggcccg 60
gcgcgagagg aggcagaggg ggcgtcaggc cgcgggagag gaggccatgg gcgcgcgcgg 120
ggcgctgctg ctggcgctgc tgctggctcg ggctggactc aggaagccgg agtcgcagga 180
```

```
ggcggcgccg ttatcaggac catgcggccg acgggtcatc acgtcgcgca tcgtgggtgg 240
agaggacgcc gaactcgggc gttggccgtg gcaggggagc ctgcgcctgt gggattccca 300
cgtatgcgga gtgagcctgc tcagccaccg ctgggcactc acggcggcgc actgctttga 360
aacctatagt gaccttagtg atccctccgg gtggatggtc cagtttggcc agctgacttc 420
catgccatcc ttctggagcc tgcaggccta ctacacccgt tacttcgtat cgaatatcta 480
tctgagccct cgctacctgg ggaattcacc ctatgacatt gccttggtga agctgtctgc 540
acctgtcacc tacactaaac acatccagcc catctgtctc caggcctcca catttgagtt 600
tgagaaccgg acagactgct gggtgactgg ctgggggtac atcaaagagg atgaggcact 660
gccatctccc cacaccctcc aggaagttca ggtcgccatc ataaacaact ctatgtgcaa 720
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tggacccttg gcctgtaaca agaatggact gtggtatcag attggagtcg tgagctgggg 840
agtgggctgt ggtcggccca atcggcccgg tgtctacacc aatatcagcc accactttga 900
gtggatccag aagctgatgg cccagagtgg catgtcccag ccagacccct cctggccgct 960
actctttttc cctcttctct gggctctccc actcctgggg ccggtctgag cctacctgag 1020
cccatgcagc ctggggccac tgccaagtca ggccctggtt ctcttctgtc ttgtttggta 1080
ataaacacat tccagttgat gccttgcagg gcattcttca aaaaaaaaaa aaaaa       1135

<210> 75
<211> 300
<212> PRT
<213> Homo sapiens

<400> 75
Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg Ala
 1               5                  10                  15
Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser Gly Pro
            20                  25                  30
Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly Glu Asp Ala
        35                  40                  45
Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg Leu Trp Asp Ser
    50                  55                  60
His Val Cys Gly Val Ser Leu Leu Ser His Arg Trp Ala Leu Thr Ala
65                  70                  75                  80
Ala His Cys Phe Glu Thr Tyr Ser Asp Leu Ser Asp Pro Ser Gly Trp
                85                  90                  95
Met Val Gln Phe Gly Gln Leu Thr Ser Met Pro Ser Phe Trp Ser Leu
            100                 105                 110
Gln Ala Tyr Tyr Thr Arg Tyr Phe Val Ser Asn Ile Tyr Leu Ser Pro
        115                 120                 125
Arg Tyr Leu Gly Asn Ser Pro Tyr Asp Ile Ala Leu Val Lys Leu Ser
    130                 135                 140
Ala Pro Val Thr Tyr Thr Lys His Ile Gln Pro Ile Cys Leu Gln Ala
145                 150                 155                 160
Ser Thr Phe Glu Phe Glu Asn Arg Thr Asp Cys Trp Val Thr Gly Trp
                165                 170                 175
Gly Tyr Ile Lys Glu Asp Glu Ala Leu Pro Ser Pro His Thr Leu Gln
            180                 185                 190
Glu Val Gln Val Ala Ile Ile Asn Asn Ser Met Cys Asn His Leu Phe
        195                 200                 205
Leu Lys Tyr Ser Phe Arg Lys Asp Ile Phe Gly Asp Met Gly Asp Ser
    210                 215                 220
Gly Gly Pro Leu Ala Cys Asn Lys Asn Gly Leu Trp Tyr Gln Ile Gly
225                 230                 235                 240
Val Val Ser Trp Gly Val Gly Cys Gly Arg Pro Asn Arg Pro Gly Val
                245                 250                 255
Tyr Thr Asn Ile Ser His His Phe Glu Trp Ile Gln Lys Leu Met Ala
            260                 265                 270
Gln Ser Gly Met Ser Gln Pro Asp Pro Ser Trp Pro Leu Leu Phe Phe
```

```
        275                 280                 285
Pro Leu Leu Trp Ala Leu Pro Leu Leu Gly Pro Val
    290                 295                 300
```

<210> 76
<211> 1194
<212> DNA
<213> Homo sapiens

<400> 76

```
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tctgctgctg ctggcgctgc ccgtcctggc gagccgcgcc tacgcggccc ctgccccagg 120
ccaggccctg cagcgagtgg gcatcgtcgg gggtcaggag gcccccagga gcaagtggcc 180
ctggcaggtg agcctgagag tccacggccc atactggatg cacttctgcg ggggctccct 240
catccacccc cagtgggtgc tgaccgcagc gcactgcgtg ggaccggacg tcaaggatct 300
ggccgccctc agggtgcaac tgcgggagca gcacctctac taccaggacc agctgctgcc 360
ggtcagcagg atcatcgtgc acccacagtt ctacaccgcc cagatcggag cggacatcgc 420
cctgctggag ctggaggagc cggtgaacgt ctccagccac gtccacacgg tcaccctgcc 480
ccctgcctca gagaccttcc ccccggggat gccgtgctgg gtcactggct ggggcgatgt 540
ggacaatgat gagcgcctcc caccgccatt tcctctgaag caggtgaagg tccccataat 600
ggaaaaccac atttgtgacg caaaatacca ccttggcgcc tacacgggag acgacgtccg 660
catcgtccgt gacgacatgc tgtgtgccgg gaacacccgg agggactcat gccagggcga 720
ctccggaggg cccctggtgt gcaaggtgaa tggcacctgg ctgcaggcgg gcgtggtcag 780
ctggggcgag ggctgtgccc agcccaaccg gcctggcatc tacacccgtg tcacctacta 840
cttggactgg atccaccact atgtccccaa aaagccgtga gtcaggcctg ggttggccac 900
ctgggtcact ggaggaccaa cccctgctgt ccaaaacacc actgcttcct acccaggtgg 960
cgactgcccc ccacaccttc cctgccccgt cctgagtgcc ccttcctgtc ctaagccccc 1020
tgctctcttc tgagcccctt cccctgtcct gaggaccctt ccctatcctg agcccccttc 1080
cctgtcctaa gcctgacgcc tgcaccgggc cctccagccc tcccctgccc agatagctgg 1140
tggtgggcgc taatcctcct gagtgctgga cctcattaaa gtgcatggaa atca       1194
```

<210> 77
<211> 275
<212> PRT
<213> Homo sapiens

<400> 77

```
Met Leu Asn Leu Leu Leu Leu Ala Leu Pro Val Leu Ala Ser Arg Ala
 1               5                  10                  15
Tyr Ala Ala Pro Ala Pro Gly Gln Ala Leu Gln Arg Val Gly Ile Val
            20                  25                  30
Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val Ser Leu
        35                  40                  45
Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser Leu Ile
    50                  55                  60
His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro Asp Val
65                  70                  75                  80
Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His Leu Tyr
                85                  90                  95
Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His Pro Gln
            100                 105                 110
Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu Leu Glu
        115                 120                 125
Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu Pro Pro
    130                 135                 140
Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr Gly Trp
145                 150                 155                 160
```

```
Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro Leu Lys
                165                 170                 175
Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala Lys Tyr
            180                 185                 190
His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg Asp Asp
        195                 200                 205
Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly Asp Ser
    210                 215                 220
Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln Ala Gly
225                 230                 235                 240
Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro Gly Ile
                245                 250                 255
Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr Val Pro
            260                 265                 270
Lys Lys Pro
        275
```

<210> 78
<211> 1528
<212> DNA
<213> Homo sapiens

<400> 78

```
ggaaggcaca ggcctgagaa gtctgcggct gagctgggag caaatccccc acccctacc 60
tgggggacag ggcaagtgag acctggtgag ggtggctcag caggaaggga aggagaggtg 120
tctgtgcgtc ctgcacccac atctttctct gtcccctcct tgccctgtct ggaggctgct 180
agactcctat cttctgaatt ctatagtgcc tgggtctcag cgcagtgccg atggtggccc 240
gtccttgtgg ttcctctcta cctggggaaa taaggtgcag cggccatggc tacagcaaga 300
ccccccctgga tgtgggtgct ctgtgctctg atcacagcct tgcttctggg ggtcacagag 360
catgttctcg ccaacaatga tgtttcctgt gaccacccct ctaacaccgt gccctctggg 420
agcaaccagg acctgggagc tggggccggg gaagacgccc ggtcggatga cagcagcagc 480
cgcatcatca atggatccga ctgcgatatg cacacccagc cgtggcaggc cgcgctgttg 540
ctaaggccca accagctcta ctgcggggcg gtgttggtgc atccacagtg gctgctcacg 600
gccgcccact gcaggaagaa agttttcaga gtccgtctcg gccactactc cctgtcacca 660
gtttatgaat ctgggcagca gatgttccag ggggtcaaat ccatcccccа ccctggctac 720
tcccaccctg gccactctaa cgacctcatg ctcatcaaac tgaacagaag aattcgtccc 780
actaaagatg tcagacccat caacgtctcc tctcattgtc cctctgctgg gacaaagtgc 840
ttggtgtctg gctgggggac aaccaagagc ccccaagtgc acttccctaa ggtcctccag 900
tgcttgaata tcagcgtgct aagtcagaaa aggtgcgagg atgcttaccc gagacagata 960
gatgacacca tgttctgcgc cggtgacaaa gcaggtagag actcctgcca gggtgattct 1020
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tgtgcccggc ccaacagacc gggtgtctac acgaacctct gcaagttcac caagtggatc 1140
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cctgctgcag ggacagccct gacactcctt tcagaccctc attccttccc agagatgttg 1260
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cacattgggc tgaccgtgtc tctctagttg aaccctggga acaatttcca aaactgtcca 1380
gggcgggggt tgcgtctcaa tctccctggg gcactttcat cctcaagctc agggcccatc 1440
ccttctctgc agctctgacc caaatttagt cccagaaata aactgagaag tggaaaaaaa 1500
aaaaaaaaaa aaaaaaaaaa aaaaaaaa                                    1528
```

<210> 79
<211> 293
<212> PRT
<213> Homo sapiens

<400> 79

```
Met Ala Thr Ala Arg Pro Pro Trp Met Trp Val Leu Cys Ala Leu Ile
```

```
 1               5                  10                  15
Thr Ala Leu Leu Leu Gly Val Thr Glu His Val Leu Ala Asn Asn Asp
            20                  25                  30
Val Ser Cys Asp His Pro Ser Asn Thr Val Pro Ser Gly Ser Asn Gln
        35                  40                  45
Asp Leu Gly Ala Gly Ala Gly Glu Asp Ala Arg Ser Asp Asp Ser Ser
    50                  55                  60
Ser Arg Ile Ile Asn Gly Ser Asp Cys Asp Met His Thr Gln Pro Trp
65                  70                  75                  80
Gln Ala Ala Leu Leu Leu Arg Pro Asn Gln Leu Tyr Cys Gly Ala Val
                85                  90                  95
Leu Val His Pro Gln Trp Leu Leu Thr Ala Ala His Cys Arg Lys Lys
            100                 105                 110
Val Phe Arg Val Arg Leu Gly His Tyr Ser Leu Ser Pro Val Tyr Glu
        115                 120                 125
Ser Gly Gln Gln Met Phe Gln Gly Val Lys Ser Ile Pro His Pro Gly
    130                 135                 140
Tyr Ser His Pro Gly His Ser Asn Asp Leu Met Leu Ile Lys Leu Asn
145                 150                 155                 160
Arg Arg Ile Arg Pro Thr Lys Asp Val Arg Pro Ile Asn Val Ser Ser
                165                 170                 175
His Cys Pro Ser Ala Gly Thr Lys Cys Leu Val Ser Gly Trp Gly Thr
            180                 185                 190
Thr Lys Ser Pro Gln Val His Phe Pro Lys Val Leu Gln Cys Leu Asn
        195                 200                 205
Ile Ser Val Leu Ser Gln Lys Arg Cys Glu Asp Ala Tyr Pro Arg Gln
    210                 215                 220
Ile Asp Asp Thr Met Phe Cys Ala Gly Asp Lys Ala Gly Arg Asp Ser
225                 230                 235                 240
Cys Gln Gly Asp Ser Gly Gly Pro Val Val Cys Asn Gly Ser Leu Gln
                245                 250                 255
Gly Leu Val Ser Trp Gly Asp Tyr Pro Cys Ala Arg Pro Asn Arg Pro
            260                 265                 270
Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Lys Trp Ile Gln Glu Thr
        275                 280                 285
Ile Gln Ala Asn Ser
    290
```

<210> 80
<211> 4942
<212> DNA
<213> Homo sapiens

<400> 80

```
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gaagagcgct gccgcagagc cgggtcccca aagccggtct tgagagctga tgacaataac 180
atgggcaatg gctgctctca gaagctggcg actgctaacc tcctccggtt cctattgctg 240
gtcctgattc catgtatctg tgctctcgtt ctcttgctgg tgatcctgct ttcctatgtt 300
ggaacattac aaaaggtcta ttttaaatca aatgggagtg aacctttggt cactgatggt 360
gaaatccaag ggtccgatgt tattcttaca aatacaattt ataaccagag cactgtggtg 420
tctactgcac atcccgacca acacgttcca gcctggacta cggatgcttc tctcccaggg 480
gaccaaagtc acaggaatac aagtgcctgt atgaacatca cccacagcca gtgtcagatg 540
ctgccctacc acgccacgct gacacctctc ctctcagttg tcagaaacat ggaaatggaa 600
aagttcctca agtttttcac atatctccat cgcctcagtt gctatcaaca tatcatgctg 660
tttggctgta ccctcgcctt ccctgagtgc atcattgatg gcgatgacag tcatggactc 720
ctgccctgta ggtccttctg tgaggctgca aaagaaggct gtgaatcagt cctggggatg 780
```

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ggaaggggtg agaactttct gtgtgccagt ggaatctgca tccccgggaa actgcaatgt 960
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ggacaatgta tccccagcac gtttcaatgt gatggtgacg aggactgcaa ggatgggagt 1320
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gagtcttctc ttttccctgc acttgttcaa accaactgtt ataaatacct catgttcttt 1620
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acttttgcca gctacactaa aagaaaatgg ccttcttgac tgtgaagagc tgcctgcaga 3300
gagctgtaca gaagcacttt tcatggacag aaatgctcaa tcgtgcactg caaatttgca 3360
tgtttgtttt ggactaattt ttttcaattt atttttcac cttcattttt ctcttatttc 3420
aagttcaatg aaagacttta caaaagcaaa caaagcagac tttgtccttt tgccaggcct 3480
aaccatgact gcagcacaaa attatcgact ctggcgagat ttaaaatcag gtgctacagt 3540
aacaggttat ggaatggtct cttttatcct atcacaaaaa aagacataga tatttaggct 3600
gattaattat ctctaccagt ttttgtttct caagctcagt gcatagtggt aaatttcagt 3660
gttaacattg gagacttgct tttctttttc ttttttata ccccacaatt ctttttatt 3720
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atgagagatg caatttttta aaaagaaaat taatttgcat ccctcgttta attaaattta 4260

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aacctaagga gagtgtgaaa tccagcaact gaattgtggt cacgattgta tgaaagttca 4800
agaacatatg tcagttttgt tacagttgta gctacatact caatgtatca acttttagcc 4860
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<210> 81
<211> 1042
<212> PRT
<213> Homo sapiens

<400> 81

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Gly Ser Pro Lys Pro Val Leu Arg Ala Asp Asp Asn Asn Met Gly Asn
            20                  25                  30
Gly Cys Ser Gln Lys Leu Ala Thr Ala Asn Leu Leu Arg Phe Leu Leu
        35                  40                  45
Leu Val Leu Ile Pro Cys Ile Cys Ala Leu Val Leu Leu Leu Val Ile
    50                  55                  60
Leu Leu Ser Tyr Val Gly Thr Leu Gln Lys Val Tyr Phe Lys Ser Asn
65                  70                  75                  80
Gly Ser Glu Pro Leu Val Thr Asp Gly Glu Ile Gln Gly Ser Asp Val
                85                  90                  95
Ile Leu Thr Asn Thr Ile Tyr Asn Gln Ser Thr Val Val Ser Thr Ala
            100                 105                 110
His Pro Asp Gln His Val Pro Ala Trp Thr Thr Asp Ala Ser Leu Pro
        115                 120                 125
Gly Asp Gln Ser His Arg Asn Thr Ser Ala Cys Met Asn Ile Thr His
    130                 135                 140
Ser Gln Cys Gln Met Leu Pro Tyr His Ala Thr Leu Thr Pro Leu Leu
145                 150                 155                 160
Ser Val Val Arg Asn Met Glu Met Glu Lys Phe Leu Lys Phe Phe Thr
                165                 170                 175
Tyr Leu His Arg Leu Ser Cys Tyr Gln His Ile Met Leu Phe Gly Cys
            180                 185                 190
Thr Leu Ala Phe Pro Glu Cys Ile Ile Asp Gly Asp Asp Ser His Gly
        195                 200                 205
Leu Leu Pro Cys Arg Ser Phe Cys Glu Ala Ala Lys Glu Gly Cys Glu
    210                 215                 220
Ser Val Leu Gly Met Val Asn Tyr Ser Trp Pro Asp Phe Leu Arg Cys
225                 230                 235                 240
Ser Gln Phe Arg Asn Gln Thr Glu Ser Ser Asn Val Ser Arg Ile Cys
                245                 250                 255
Phe Ser Pro Gln Gln Glu Asn Gly Lys Gln Leu Leu Cys Gly Arg Gly
            260                 265                 270
Glu Asn Phe Leu Cys Ala Ser Gly Ile Cys Ile Pro Gly Lys Leu Gln
        275                 280                 285
Cys Asn Gly Tyr Asn Asp Cys Asp Asp Trp Ser Asp Glu Ala His Cys
    290                 295                 300
Asn Cys Ser Glu Asn Leu Phe His Cys His Thr Gly Lys Cys Leu Asn
```

305 310 315 320
Tyr Ser Leu Val Cys Asp Gly Tyr Asp Asp Cys Gly Asp Leu Ser Asp
325 330 335
Glu Gln Asn Cys Asp Cys Asn Pro Thr Thr Glu His Arg Cys Gly Asp
340 345 350
Gly Arg Cys Ile Ala Met Glu Trp Val Cys Asp Gly Asp His Asp Cys
355 360 365
Val Asp Lys Ser Asp Glu Val Asn Cys Ser Cys His Ser Gln Gly Leu
370 375 380
Val Glu Cys Arg Asn Gly Gln Cys Ile Pro Ser Thr Phe Gln Cys Asp
385 390 395 400
Gly Asp Glu Asp Cys Lys Asp Gly Ser Asp Glu Glu Asn Cys Ser Val
405 410 415
Ile Gln Thr Ser Cys Gln Glu Gly Asp Gln Arg Cys Leu Tyr Asn Pro
420 425 430
Cys Leu Asp Ser Cys Gly Gly Ser Ser Leu Cys Asp Pro Asn Asn Ser
435 440 445
Leu Asn Asn Cys Ser Gln Cys Glu Pro Ile Thr Leu Glu Leu Cys Met
450 455 460
Asn Leu Pro Tyr Asn Ser Thr Ser Tyr Pro Asn Tyr Phe Gly His Arg
465 470 475 480
Thr Gln Lys Glu Ala Ser Ile Ser Trp Glu Ser Ser Leu Phe Pro Ala
485 490 495
Leu Val Gln Thr Asn Cys Tyr Lys Tyr Leu Met Phe Phe Ser Cys Thr
500 505 510
Ile Leu Val Pro Lys Cys Asp Val Asn Thr Gly Glu His Ile Pro Pro
515 520 525
Cys Arg Ala Leu Cys Glu His Ser Lys Glu Arg Cys Glu Ser Val Leu
530 535 540
Gly Ile Val Gly Leu Gln Trp Pro Glu Asp Thr Asp Cys Ser Gln Phe
545 550 555 560
Pro Glu Glu Asn Ser Asp Asn Gln Thr Cys Leu Met Pro Asp Glu Tyr
565 570 575
Val Glu Glu Cys Ser Pro Ser His Phe Lys Cys Arg Ser Gly Gln Cys
580 585 590
Val Leu Ala Ser Arg Arg Cys Asp Gly Gln Ala Asp Cys Asp Asp Asp
595 600 605
Ser Asp Glu Glu Asn Cys Gly Cys Lys Glu Arg Asp Leu Trp Glu Cys
610 615 620
Pro Ser Asn Lys Gln Cys Leu Lys His Thr Val Ile Cys Asp Gly Phe
625 630 635 640
Pro Asp Cys Pro Asp Tyr Met Asp Glu Lys Asn Cys Ser Phe Cys Gln
645 650 655
Asp Asp Glu Leu Glu Cys Ala Asn His Ala Cys Val Ser Arg Asp Leu
660 665 670
Trp Cys Asp Gly Glu Ala Asp Cys Ser Asp Ser Ser Asp Glu Trp Asp
675 680 685
Cys Val Thr Leu Ser Ile Asn Val Asn Ser Ser Ser Phe Leu Met Val
690 695 700
His Arg Ala Ala Thr Glu His His Val Cys Ala Asp Gly Trp Gln Glu
705 710 715 720
Ile Leu Ser Gln Leu Ala Cys Lys Gln Met Gly Leu Gly Glu Pro Ser
725 730 735
Val Thr Lys Leu Ile Gln Glu Gln Glu Lys Glu Pro Arg Trp Leu Thr
740 745 750
Leu His Ser Asn Trp Glu Ser Leu Asn Gly Thr Thr Leu His Glu Leu
755 760 765
Leu Val Asn Gly Gln Ser Cys Glu Ser Arg Ser Lys Ile Ser Leu Leu

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    770                 775                 780
Cys Thr Lys Gln Asp Cys Gly Arg Arg Pro Ala Ala Arg Met Asn Lys
785                 790                 795                 800
Arg Ile Leu Gly Gly Arg Thr Ser Arg Pro Gly Arg Trp Pro Trp Gln
                805                 810                 815
Cys Ser Leu Gln Ser Glu Pro Ser Gly His Ile Cys Gly Cys Val Leu
            820                 825                 830
Ile Ala Lys Lys Trp Val Leu Thr Val Ala His Cys Phe Glu Gly Arg
        835                 840                 845
Glu Asn Ala Ala Val Trp Lys Val Val Leu Gly Ile Asn Asn Leu Asp
    850                 855                 860
His Pro Ser Val Phe Met Gln Thr Arg Phe Val Lys Thr Ile Ile Leu
865                 870                 875                 880
His Pro Arg Tyr Ser Arg Ala Val Val Asp Tyr Asp Ile Ser Ile Val
                885                 890                 895
Glu Leu Ser Glu Asp Ile Ser Glu Thr Gly Tyr Val Arg Pro Val Cys
            900                 905                 910
Leu Pro Asn Pro Glu Gln Trp Leu Glu Pro Asp Thr Tyr Cys Tyr Ile
        915                 920                 925
Thr Gly Trp Gly His Met Gly Asn Lys Met Pro Phe Lys Leu Gln Glu
    930                 935                 940
Gly Glu Val Arg Ile Ile Ser Leu Glu His Cys Gln Ser Tyr Phe Asp
945                 950                 955                 960
Met Lys Thr Ile Thr Thr Arg Met Ile Cys Ala Gly Tyr Glu Ser Gly
                965                 970                 975
Thr Val Asp Ser Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Glu
            980                 985                 990
Lys Pro Gly Gly Arg Trp Thr Leu Phe Gly Leu Thr Ser Trp Gly Ser
        995                 1000                1005
Val Cys Phe Ser Lys Val Leu Gly Pro Gly Val Tyr Ser Asn Val Ser
    1010                1015                1020
Tyr Phe Val Glu Trp Ile Lys Arg Gln Ile Tyr Ile Gln Thr Phe Leu
1025                1030                1035                1040
Leu Asn
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<210> 82
<211> 945
<212> DNA
<213> Homo sapiens

<400> 82

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gggctcagca tctttttgct cctgtgtgtt cttgggctca gccaggcagc cacaccgaag 180
attttcaatg gcactgagtg tgggcgtaac tcacagccgt ggcaggtggg gctgtttgag 240
ggcaccagcc tgcgctgcgg gggtgtcctt attgaccaca ggtgggtcct cacagcggct 300
cactgcagcg gcagcaggta ctgggtgcgc ctgggggaac acagcctcag ccagctcgac 360
tggaccgagc agatccggca cagcggcttc tctgtgaccc atcccggcta cctgggagcc 420
tcgacgagcc acgagcacga cctccggctg ctgcggctgc gcctgcccgt ccgcgtaacc 480
agcagcgttc aacccctgcc cctgcccaat gactgtgcaa ccgctggcac cgagtgccac 540
gtctcaggct ggggcatcac caaccaccca cggaacccat tcccggatct gctccagtgc 600
ctcaacctct ccatcgtctc ccatgccacc tgccatggtg tgtatcccgg gagaatcacg 660
agcaacatgg tgtgtgcagg cggcgtcccg gggcaggatg cctgccaggg tgattctggg 720
ggcccctgg tgtgtggggg agtccttcaa ggtctggtgt cctgggggtc tgtggggccc 780
tgtggacaag atggcatccc tggagtctac acctatattt gcaactccac tcttgttggc 840
ctgggaactt cttggaactt taactcctgc cagcccttct aagacccacg agcggggtga 900
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gagaagtgtg caatagtctg gaataaatat aaatgaagga ggggc 945

<210> 83
<211> 254
<212> PRT
<213> Homo sapiens

<400> 83
Met Gly Leu Ser Ile Phe Leu Leu Leu Cys Val Leu Gly Leu Ser Gln
1 5 10 15
Ala Ala Thr Pro Lys Ile Phe Asn Gly Thr Glu Cys Gly Arg Asn Ser
20 25 30
Gln Pro Trp Gln Val Gly Leu Phe Glu Gly Thr Ser Leu Arg Cys Gly
35 40 45
Gly Val Leu Ile Asp His Arg Trp Val Leu Thr Ala Ala His Cys Ser
50 55 60
Gly Ser Arg Tyr Trp Val Arg Leu Gly Glu His Ser Leu Ser Gln Leu
65 70 75 80
Asp Trp Thr Glu Gln Ile Arg His Ser Gly Phe Ser Val Thr His Pro
85 90 95
Gly Tyr Leu Gly Ala Ser Thr Ser His Glu His Asp Leu Arg Leu Leu
100 105 110
Arg Leu Arg Leu Pro Val Arg Val Thr Ser Ser Val Gln Pro Leu Pro
115 120 125
Leu Pro Asn Asp Cys Ala Thr Ala Gly Thr Glu Cys His Val Ser Gly
130 135 140
Trp Gly Ile Thr Asn His Pro Arg Asn Pro Phe Pro Asp Leu Leu Gln
145 150 155 160
Cys Leu Asn Leu Ser Ile Val Ser His Ala Thr Cys His Gly Val Tyr
165 170 175
Pro Gly Arg Ile Thr Ser Asn Met Val Cys Ala Gly Gly Val Pro Gly
180 185 190
Gln Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Gly
195 200 205
Val Leu Gln Gly Leu Val Ser Trp Gly Ser Val Gly Pro Cys Gly Gln
210 215 220
Asp Gly Ile Pro Gly Val Tyr Thr Tyr Ile Cys Asn Ser Thr Leu Val
225 230 235 240
Gly Leu Gly Thr Ser Trp Asn Phe Asn Ser Cys Gln Pro Phe
245 250

<210> 84
<211> 1074
<212> DNA
<213> Homo sapiens

<400> 84
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gggctcagca tctttttgct cctgtgtgtt cttgggctca gccaggcagc cacaccgaag 180
attttcaatg gcactgagtg tgggcgtaac tcacagccgt ggcaggtggg gctgtttgag 240
ggcaccagcc tgcgctgcgg gggtgtcctt attgaccaca ggtgggtcct cacagcggct 300
cactgcagcg gcagcaggta ctgggtgcgc ctgggggaac acagcctcag ccagctcgac 360
tggaccgagc agatccggca cagcggcttc tctgtgaccc atcccggcta cctgggagcc 420
tcgacgagcc acgagcacga cctccggctg ctgcggctgc gcctgcccgt ccgcgtaacc 480
agcagcgttc aacccctgcc cctgcccaat gactgtgcaa ccgctggcac cgagtgccac 540
gtctcaggct ggggcatcac caaccaccca cggaacccat tcccggatct gctccagtgc 600

ctcaacctct ccatcgtctc ccatgccacc tgccatggtg tgtatcccgg gagaatcacg 660
agcaacatgg tgtgtgcagg cggcgtcccg gggcaggatg cctgccaggg tgattctggg 720
ggcccccctgg tgtgtggggg agtccttcaa ggtctggtgt cctgggggtc tgtggggccc 780
tgtggacaag atggcatccc tggagtctac acctatattt gcaagtatgt ggactggatc 840
cggatgatca tgaggaacaa ctgacctgtt tcctccacct ccacccccac cccttaactt 900
gggtaccect ctggccctca gagcaccaat atctcctcca tcacttcccc tagctccact 960
cttgttggcc tgggaacttc ttggaacttt aactcctgcc agcccttcta agacccacga 1020
gcggggtgag agaagtgtgc aatagtctgg aataaatata aatgaaggag gggc 1074

<210> 85
<211> 248
<212> PRT
<213> Homo sapiens

<400> 85
Met Gly Leu Ser Ile Phe Leu Leu Leu Cys Val Leu Gly Leu Ser Gln
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20 25 30
Gln Pro Trp Gln Val Gly Leu Phe Glu Gly Thr Ser Leu Arg Cys Gly
35 40 45
Gly Val Leu Ile Asp His Arg Trp Val Leu Thr Ala Ala His Cys Ser
50 55 60
Gly Ser Arg Tyr Trp Val Arg Leu Gly Glu His Ser Leu Ser Gln Leu
65 70 75 80
Asp Trp Thr Glu Gln Ile Arg His Ser Gly Phe Ser Val Thr His Pro
85 90 95
Gly Tyr Leu Gly Ala Ser Thr Ser His Glu His Asp Leu Arg Leu Leu
100 105 110
Arg Leu Arg Leu Pro Val Arg Val Thr Ser Ser Val Gln Pro Leu Pro
115 120 125
Leu Pro Asn Asp Cys Ala Thr Ala Gly Thr Glu Cys His Val Ser Gly
130 135 140
Trp Gly Ile Thr Asn His Pro Arg Asn Pro Phe Pro Asp Leu Leu Gln
145 150 155 160
Cys Leu Asn Leu Ser Ile Val Ser His Ala Thr Cys His Gly Val Tyr
165 170 175
Pro Gly Arg Ile Thr Ser Asn Met Val Cys Ala Gly Gly Val Pro Gly
180 185 190
Gln Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Gly
195 200 205
Val Leu Gln Gly Leu Val Ser Trp Gly Ser Val Gly Pro Cys Gly Gln
210 215 220
Asp Gly Ile Pro Gly Val Tyr Thr Tyr Ile Cys Lys Tyr Val Asp Trp
225 230 235 240
Ile Arg Met Ile Met Arg Asn Asn
245

<210> 86
<211> 814
<212> DNA
<213> Homo sapiens

<400> 86
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gggctcagca tctttttgct cctgtgtgtt cttgggctca gccaggcagc cacaccgaag 180

attttcaatg gcactgagtg tgggcgtaac tcacagccgt ggcaggtggg gctgtttgag 240
ggcaccagcc tgcgctgcgg gggtgtcctt attgaccaca ggtgggtcct cacagcggct 300
cactgcagcg gcagacccat tcccggatct gctccagtgc ctcaacctct ccatcgtctc 360
ccatgccacc tgccatggtg tgtatcccgg gagaatcacg agcaacatgg tgtgtgcagg 420
cggcgtcccg gggcaggatg cctgccaggg tgattctggg ggccccctgg tgtgtggggg 480
agtccttcaa ggtctggtgt cctgggggtc tgtggggccc tgtggacaag atggcatccc 540
tggagtctac acctatattt gcaagtatgt ggactggatc cggatgatca tgaggaacaa 600
ctgacctgtt tcctccacct ccacccccac cccttaactt gggtaccect ctggccctca 660
gagcaccaat atctcctcca tcacttcccc tagctccact cttgttggcc tgggaacttc 720
ttggaacttt aactcctgcc agcccttcta agacccacga gcggggtgag agaagtgtgc 780
aatagtctgg aataaatata aatgaaggag gggc 814

<210> 87
<211> 111
<212> PRT
<213> Homo sapiens

<400> 87
Met Gly Leu Ser Ile Phe Leu Leu Leu Cys Val Leu Gly Leu Ser Gln
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Ala Ala Thr Pro Lys Ile Phe Asn Gly Thr Glu Cys Gly Arg Asn Ser
            20   25   30
Gln Pro Trp Gln Val Gly Leu Phe Glu Gly Thr Ser Leu Arg Cys Gly
        35   40   45
Gly Val Leu Ile Asp His Arg Trp Val Leu Thr Ala Ala His Cys Ser
    50   55   60
Gly Arg Pro Ile Pro Gly Ser Ala Pro Val Pro Gln Pro Leu His Arg
65   70   75   80
Leu Pro Cys His Leu Pro Trp Cys Val Ser Arg Glu Asn His Glu Gln
                85   90   95
His Gly Val Cys Arg Arg Arg Pro Gly Ala Gly Cys Leu Pro Gly
            100   105   110

<210> 88
<211> 1471
<212> DNA
<213> Homo sapiens

<400> 88
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tcggccagat gtggtgaggg ctaggaaaag agtttgttgg gaaccctggg ttatcggcct 120
cgtcatcttc atatccctga ttgtcctggc agtgtgcatt ggactcactg ttcattatgt 180
gagatataat caaaagaaga cctacaatta ctatagcaca ttgtcattta caactgacaa 240
actatatgct gagtttggca gagaggcttc taacaatttt acagaaatga gccagagact 300
tgaatcaatg gtgaaaaatg cattttataa atctccatta agggaagaat ttgtcaagtc 360
tcaggttatc aagttcagtc aacagaagca tggagtgttg gctcatatgc tgttgatttg 420
tagatttcac tctactgagg atcctgaaac tgtagataaa attgttcaac ttgttttaca 480
tgaaaagctg caagatgctg taggacccca taaagtagat cctcactcag ttaaaattaa 540
aaaaatcaac aagacagaaa cagacagcta tctaaaccat tgctgcggaa cacgaagaag 600
taaaactcta ggtcagagtc tcaggatcgt tggtgggaca gaagtagaag agggtgaatg 660
gccctggcag gctagcctgc agtgggatgg gagtcatcgc tgtggagcaa ccttaattaa 720
tgccacatgg cttgtgagtg ctgctcactg ttttacaaca tataagaacc ctgccagatg 780
gactgcttcc tttggagtaa caataaaacc ttcgaaaatg aaacggggtc tccggagaat 840
aattgtccat gaaaaataca aacacccatc acatgactat gatatttctc ttgcagagct 900
ttctagccct gttccctaca caaatgcagt acatagagtt tgtctccctg atgcatccta 960
tgagtttcaa ccaggtgatg tgatgtttgt gacaggattt ggagcactga aaaatgatgg 1020
ttacagtcaa aatcatcttc gacaagcaca ggtgactctc atagacgcta caacttgcaa 1080

tgaacctcaa gcttacaatg acgccataac tcctagaatg ttatgtgctg gctccttaga 1140
aggaaaaaca gatgcatgcc agggtgactc tggaggacca ctggttagtt cagatgctag 1200
agatatctgg taccttgctg gaatagtgag ctggggagat gaatgtgcga aacccaacaa 1260
gcctggtgtt tatactagag ttacggcctt gcgggactgg attacttcaa aaactggtat 1320
ctaagagaga aaagcctcat ggaacagata acatttttt ttgtttttg ggtgtggagg 1380
ccatttttag agatacagaa ttggagaaga cttgcaaaac agctagattt gactgatctc 1440
aataaactgt ttgcttgatg caaaaaaaaa a 1471

<210> 89
<211> 422
<212> PRT
<213> Homo sapiens

<400> 89

Met	Tyr	Arg	Pro	Asp	Val	Val	Arg	Ala	Arg	Lys	Arg	Val	Cys	Trp	Glu
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Pro	Trp	Val	Ile	Gly	Leu	Val	Ile	Phe	Ile	Ser	Leu	Ile	Val	Leu	Ala
			20					25					30		
Val	Cys	Ile	Gly	Leu	Thr	Val	His	Tyr	Val	Arg	Tyr	Asn	Gln	Lys	Lys
		35					40					45			
Thr	Tyr	Asn	Tyr	Tyr	Ser	Thr	Leu	Ser	Phe	Thr	Thr	Asp	Lys	Leu	Tyr
	50					55					60				
Ala	Glu	Phe	Gly	Arg	Glu	Ala	Ser	Asn	Asn	Phe	Thr	Glu	Met	Ser	Gln
65					70					75					80
Arg	Leu	Glu	Ser	Met	Val	Lys	Asn	Ala	Phe	Tyr	Lys	Ser	Pro	Leu	Arg
				85					90					95	
Glu	Glu	Phe	Val	Lys	Ser	Gln	Val	Ile	Lys	Phe	Ser	Gln	Gln	Lys	His
			100					105					110		
Gly	Val	Leu	Ala	His	Met	Leu	Leu	Ile	Cys	Arg	Phe	His	Ser	Thr	Glu
		115					120					125			
Asp	Pro	Glu	Thr	Val	Asp	Lys	Ile	Val	Gln	Leu	Val	Leu	His	Glu	Lys
	130					135					140				
Leu	Gln	Asp	Ala	Val	Gly	Pro	Pro	Lys	Val	Asp	Pro	His	Ser	Val	Lys
145					150					155					160
Ile	Lys	Lys	Ile	Asn	Lys	Thr	Glu	Thr	Asp	Ser	Tyr	Leu	Asn	His	Cys
				165					170					175	
Cys	Gly	Thr	Arg	Arg	Ser	Lys	Thr	Leu	Gly	Gln	Ser	Leu	Arg	Ile	Val
			180					185					190		
Gly	Gly	Thr	Glu	Val	Glu	Glu	Gly	Glu	Trp	Pro	Trp	Gln	Ala	Ser	Leu
		195					200					205			
Gln	Trp	Asp	Gly	Ser	His	Arg	Cys	Gly	Ala	Thr	Leu	Ile	Asn	Ala	Thr
	210					215					220				
Trp	Leu	Val	Ser	Ala	Ala	His	Cys	Phe	Thr	Thr	Tyr	Lys	Asn	Pro	Ala
225					230					235					240
Arg	Trp	Thr	Ala	Ser	Phe	Gly	Val	Thr	Ile	Lys	Pro	Ser	Lys	Met	Lys
				245					250					255	
Arg	Gly	Leu	Arg	Arg	Ile	Ile	Val	His	Glu	Lys	Tyr	Lys	His	Pro	Ser
			260					265					270		
His	Asp	Tyr	Asp	Ile	Ser	Leu	Ala	Glu	Leu	Ser	Ser	Pro	Val	Pro	Tyr
		275					280					285			
Thr	Asn	Ala	Val	His	Arg	Val	Cys	Leu	Pro	Asp	Ala	Ser	Tyr	Glu	Phe
	290					295					300				
Gln	Pro	Gly	Asp	Val	Met	Phe	Val	Thr	Gly	Phe	Gly	Ala	Leu	Lys	Asn
305					310					315					320
Asp	Gly	Tyr	Ser	Gln	Asn	His	Leu	Arg	Gln	Ala	Gln	Val	Thr	Leu	Ile
				325					330					335	
Asp	Ala	Thr	Thr	Cys	Asn	Glu	Pro	Gln	Ala	Tyr	Asn	Asp	Ala	Ile	Thr
			340					345					350		

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Pro Arg Met Leu Cys Ala Gly Ser Leu Glu Gly Lys Thr Asp Ala Cys
        355                 360                 365
Gln Gly Asp Ser Gly Gly Pro Leu Val Ser Ser Asp Ala Arg Asp Ile
    370                 375                 380
Trp Tyr Leu Ala Gly Ile Val Ser Trp Gly Asp Glu Cys Ala Lys Pro
385                 390                 395                 400
Asn Lys Pro Gly Val Tyr Thr Arg Val Thr Ala Leu Arg Asp Trp Ile
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Thr Ser Lys Thr Gly Ile
            420
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<210> 90
<211> 1124
<212> DNA
<213> Homo sapiens

<400> 90
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ggggtcacgc tgccccggcc ggcgcatggc catggcaggc cagcctccgc ctgcggagga 180
tgcacgtgtg cggcgggtca ctgctcagcc cccagtgggt gctcacagct gcccactgct 240
tctccgggtc cctgaactca tccgactacc aggtgcacct gggggaactg gagatcactt 300
tgtctcccca cttctccacc gtgaggcaga tcatcctgca ctccagcccc tcaggacagc 360
cggggaccag cggggacatc gccctggtgg agctcagtgt ccccgtgacc ctctccagcc 420
ggatcctgcc cgtctgcctc ccggaggcct cagatgactt ctgccctggg atccggtgct 480
gggtgaccgg ctggggctat acgcgggagg gagagcctct gccacccccg tacagcctgc 540
gggaggtgaa agtctccgtg gtggacacag agacctgccg ccgggactat cccggccccg 600
ggggcagcat ccttcagccc gacatgctgt gtgccccggg ccccggggat gcctgccagg 660
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tgagctgggg tgagggctgc ggccgcccca acaggccggg agtctacact cgtgtccctg 780
cctacgtgaa ctggatccgc cgccacatca cagcatcagg gggctcagag tctgggtacc 840
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gtgtcctgct ggccaagtgc ctgctgcacc catctgcgga tggtactccc ttccccgccc 960
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tgaatttaaa agcacacgaa acaaaaaaaa aaaaaaaaaa aaaa 1124

<210> 91
<211> 321
<212> PRT
<213> Homo sapiens

<400> 91
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 1               5                  10                  15
Val Ser Leu Arg Thr Leu Gln Pro Gly Cys Gly Arg Pro Gln Val Ser
            20                  25                  30
Asp Ala Gly Gly Arg Ile Val Gly Gly His Ala Ala Pro Ala Gly Ala
        35                  40                  45
Trp Pro Trp Gln Ala Ser Leu Arg Leu Arg Arg Met His Val Cys Gly
    50                  55                  60
Gly Ser Leu Leu Ser Pro Gln Trp Val Leu Thr Ala Ala His Cys Phe
65                  70                  75                  80
Ser Gly Ser Leu Asn Ser Ser Asp Tyr Gln Val His Leu Gly Glu Leu
                85                  90                  95
Glu Ile Thr Leu Ser Pro His Phe Ser Thr Val Arg Gln Ile Ile Leu
            100                 105                 110
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His Ser Ser Pro Ser Gly Gln Pro Gly Thr Ser Gly Asp Ile Ala Leu
        115                 120                 125
Val Glu Leu Ser Val Pro Val Thr Leu Ser Ser Arg Ile Leu Pro Val
    130                 135                 140
Cys Leu Pro Glu Ala Ser Asp Asp Phe Cys Pro Gly Ile Arg Cys Trp
145                 150                 155                 160
Val Thr Gly Trp Gly Tyr Thr Arg Glu Gly Glu Pro Leu Pro Pro Pro
                165                 170                 175
Tyr Ser Leu Arg Glu Val Lys Val Ser Val Val Asp Thr Glu Thr Cys
            180                 185                 190
Arg Arg Asp Tyr Pro Gly Pro Gly Gly Ser Ile Leu Gln Pro Asp Met
        195                 200                 205
Leu Cys Ala Arg Gly Pro Gly Asp Ala Cys Gln Asp Asp Ser Gly Gly
    210                 215                 220
Pro Leu Val Cys Gln Val Asn Gly Ala Trp Val Gln Ala Gly Ile Val
225                 230                 235                 240
Ser Trp Gly Glu Gly Cys Gly Arg Pro Asn Arg Pro Gly Val Tyr Thr
                245                 250                 255
Arg Val Pro Ala Tyr Val Asn Trp Ile Arg Arg His Ile Thr Ala Ser
            260                 265                 270
Gly Gly Ser Glu Ser Gly Tyr Pro Arg Leu Pro Leu Leu Ala Gly Phe
        275                 280                 285
Phe Leu Pro Gly Leu Phe Leu Leu Leu Val Ser Cys Val Leu Leu Ala
    290                 295                 300
Lys Cys Leu Leu His Pro Ser Ala Asp Gly Thr Pro Phe Pro Ala Pro
305                 310                 315                 320
Asp
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<210> 92
<211> 1459
<212> DNA
<213> Homo sapiens

<400> 92

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gggacctgtg ccctgctcca catcctccca cctgccgccc gcagagcctg caggccccgc 180
ccccctcgtc tctggtcccc acctctctgc tgtgtcttca tgtccctgag ggtcttgggc 240
tctgggacct ggccctcagc ccctaaaatg ttcctcctgc tgacagcact tcaagtcctg 300
gctatagcca tgacacagag ccaagaggat gagaacaaga taattggtgg ccatacgtgc 360
acccggagct cccagccgtg gcaggcggcc ctgctggcgg gtcccaggcg ccgcttcctc 420
tgcggaggcg ccctgctttc aggccagtgg gtcatcactg ctgctcactg cggccgcccg 480
atccttcagg ttgccctggg caagcacaac ctgaggaggt gggaggccac ccagcaggtg 540
ctgcgcgtgg ttcgtcaggt gacgcacccc aactacaact cccggaccca cgacaacgac 600
ctcatgctgc tgcagctaca gcagcccgca cggatcggga gggcagtcag gcccattgag 660
gtcacccagg cctgtgccag ccccgggacc tcctgccgag tgtcaggctg gggaactata 720
tccagcccca tcgccaggta ccccgcctct ctgcaatgcg tgaacatcaa catctccccg 780
gatgaggtgt gccagaaggc ctatcctaga accatcacgc ctggcatggt ctgtgcagga 840
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gccccagtcc ccagcatcct gatctttact ccggctctga tctctccttt cccagagcag 1260
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aagaccggag gcacagaggg caggagcaca gacccttaa accggcattg tattccaaag 1380
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ggaatcatcc taaattgta 1459

<210> 93
<211> 251
<212> PRT
<213> Homo sapiens

<400> 93

Met	Phe	Leu	Leu	Leu	Thr	Ala	Leu	Gln	Val	Leu	Ala	Ile	Ala	Met	Thr
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Gln	Ser	Gln	Glu	Asp	Glu	Asn	Lys	Ile	Ile	Gly	Gly	His	Thr	Cys	Thr
			20					25					30		
Arg	Ser	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu	Leu	Ala	Gly	Pro	Arg	Arg
		35					40					45			
Arg	Phe	Leu	Cys	Gly	Gly	Ala	Leu	Leu	Ser	Gly	Gln	Trp	Val	Ile	Thr
	50					55					60				
Ala	Ala	His	Cys	Gly	Arg	Pro	Ile	Leu	Gln	Val	Ala	Leu	Gly	Lys	His
65					70					75					80
Asn	Leu	Arg	Arg	Trp	Glu	Ala	Thr	Gln	Gln	Val	Leu	Arg	Val	Val	Arg
				85					90					95	
Gln	Val	Thr	His	Pro	Asn	Tyr	Asn	Ser	Arg	Thr	His	Asp	Asn	Asp	Leu
			100					105					110		
Met	Leu	Leu	Gln	Leu	Gln	Gln	Pro	Ala	Arg	Ile	Gly	Arg	Ala	Val	Arg
		115					120					125			
Pro	Ile	Glu	Val	Thr	Gln	Ala	Cys	Ala	Ser	Pro	Gly	Thr	Ser	Cys	Arg
	130					135					140				
Val	Ser	Gly	Trp	Gly	Thr	Ile	Ser	Ser	Pro	Ile	Ala	Arg	Tyr	Pro	Ala
145					150					155					160
Ser	Leu	Gln	Cys	Val	Asn	Ile	Asn	Ile	Ser	Pro	Asp	Glu	Val	Cys	Gln
				165					170					175	
Lys	Ala	Tyr	Pro	Arg	Thr	Ile	Thr	Pro	Gly	Met	Val	Cys	Ala	Gly	Val
			180					185					190		
Pro	Gln	Gly	Gly	Lys	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu
		195					200					205			
Val	Cys	Arg	Gly	Gln	Leu	Gln	Gly	Leu	Val	Ser	Trp	Gly	Met	Glu	Arg
	210					215					220				
Cys	Ala	Leu	Pro	Gly	Tyr	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Tyr
225					230					235					240
Arg	Ser	Trp	Ile	Glu	Glu	Thr	Met	Arg	Asp	Lys					
				245					250						

<210> 94
<211> 3008
<212> DNA
<213> Homo sapiens

<400> 94
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catgttctgc tgttaatggc tctggtggga aagacagcct gtgggttctc cctgatgtct 180
ttattggaaa gcctggaccc agactggacc cctgaccagt atgattacag ctacgaggat 240
tataatcagg aagagaacac cagtagcaca cttacccacg ctgagaatcc tgactggtac 300
tacactgagg accaagctga tccatgccag cccaaccct gtgaacacgg tggggactgc 360
ctcgtccatg ggagcacctt cacatgcagc tgcctggctc ctttctctgg gaataagtgt 420
cagaaagtgc aaaatacgtg caaggacaac ccatgtggcc ggggccaatg tctcattacc 480

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cagagtcctc cctactaccg ctgtgtctgt aaacaccctt acacaggtcc cagctgctcc 540
caagtggttc ctgtatgcag gccaaacccc tgccagaatg gggctacctg ctcccggcat 600
aagcggagat ccaagttcac ctgtgcctgt cccgaccagt tcaaggggaa attctgtgaa 660
ataggttctg atgactgcta tgttggcgat ggctactctt accgagggaa aatgaatagg 720
acagtcaacc agcatgcgtg cctttactgg aactcccacc tcctcttgca ggagaattac 780
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ttgaaaag                                                        3008

<210> 95
<211> 560
<212> PRT
<213> Homo sapiens

<400> 95
Met Phe Ala Arg Met Ser Asp Leu His Val Leu Leu Leu Met Ala Leu
 1               5                  10                  15
Val Gly Lys Thr Ala Cys Gly Phe Ser Leu Met Ser Leu Leu Glu Ser
            20                  25                  30
Leu Asp Pro Asp Trp Thr Pro Asp Gln Tyr Asp Tyr Ser Tyr Glu Asp
        35                  40                  45
Tyr Asn Gln Glu Glu Asn Thr Ser Ser Thr Leu Thr His Ala Glu Asn
    50                  55                  60
```

```
Pro Asp Trp Tyr Tyr Thr Glu Asp Gln Ala Asp Pro Cys Gln Pro Asn
65                  70                  75                  80
Pro Cys Glu His Gly Gly Asp Cys Leu Val His Gly Ser Thr Phe Thr
                85                  90                  95
Cys Ser Cys Leu Ala Pro Phe Ser Gly Asn Lys Cys Gln Lys Val Gln
            100                 105                 110
Asn Thr Cys Lys Asp Asn Pro Cys Gly Arg Gly Gln Cys Leu Ile Thr
        115                 120                 125
Gln Ser Pro Pro Tyr Tyr Arg Cys Val Cys Lys His Pro Tyr Thr Gly
    130                 135                 140
Pro Ser Cys Ser Gln Val Val Pro Val Cys Arg Pro Asn Pro Cys Gln
145                 150                 155                 160
Asn Gly Ala Thr Cys Ser Arg His Lys Arg Arg Ser Lys Phe Thr Cys
                165                 170                 175
Ala Cys Pro Asp Gln Phe Lys Gly Lys Phe Cys Glu Ile Gly Ser Asp
            180                 185                 190
Asp Cys Tyr Val Gly Asp Gly Tyr Ser Tyr Arg Gly Lys Met Asn Arg
        195                 200                 205
Thr Val Asn Gln His Ala Cys Leu Tyr Trp Asn Ser His Leu Leu Leu
    210                 215                 220
Gln Glu Asn Tyr Asn Met Phe Met Glu Asp Ala Glu Thr His Gly Ile
225                 230                 235                 240
Gly Glu His Asn Phe Cys Arg Asn Pro Asp Ala Asp Glu Lys Pro Trp
                245                 250                 255
Cys Phe Ile Lys Val Thr Asn Asp Lys Val Lys Trp Glu Tyr Cys Asp
            260                 265                 270
Val Ser Ala Cys Ser Ala Gln Asp Val Ala Tyr Pro Glu Glu Ser Pro
        275                 280                 285
Thr Glu Pro Ser Thr Lys Leu Pro Gly Phe Asp Ser Cys Gly Lys Thr
    290                 295                 300
Glu Ile Ala Glu Arg Lys Ile Lys Arg Ile Tyr Gly Gly Phe Lys Ser
305                 310                 315                 320
Thr Ala Gly Lys His Pro Trp Gln Ala Ser Leu Gln Ser Ser Leu Pro
                325                 330                 335
Leu Thr Ile Ser Met Pro Gln Gly His Phe Cys Gly Gly Ala Leu Ile
            340                 345                 350
His Pro Cys Trp Val Leu Thr Ala Ala His Cys Thr Asp Ile Lys Thr
        355                 360                 365
Arg His Leu Lys Val Val Leu Gly Asp Gln Asp Leu Lys Lys Glu Glu
    370                 375                 380
Phe His Glu Gln Ser Phe Arg Val Glu Lys Ile Phe Lys Tyr Ser His
385                 390                 395                 400
Tyr Asn Glu Arg Asp Glu Ile Pro His Asn Asp Ile Ala Leu Leu Lys
                405                 410                 415
Leu Lys Pro Val Asp Gly His Cys Ala Leu Glu Ser Lys Tyr Val Lys
            420                 425                 430
Thr Val Cys Leu Pro Asp Gly Ser Phe Pro Ser Gly Ser Glu Cys His
        435                 440                 445
Ile Ser Gly Trp Gly Val Thr Glu Thr Gly Lys Gly Ser Arg Gln Leu
    450                 455                 460
Leu Asp Ala Lys Val Lys Leu Ile Ala Asn Thr Leu Cys Asn Ser Arg
465                 470                 475                 480
Gln Leu Tyr Asp His Met Ile Asp Asp Ser Met Ile Cys Ala Gly Asn
                485                 490                 495
Leu Gln Lys Pro Gly Gln Asp Thr Cys Gln Gly Asp Ser Gly Gly Pro
            500                 505                 510
Leu Thr Cys Glu Lys Asp Gly Thr Tyr Tyr Val Tyr Gly Ile Val Ser
        515                 520                 525
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```
Trp Gly Leu Glu Cys Gly Lys Arg Pro Gly Val Tyr Thr Gln Val Thr
    530                 535                 540
Lys Phe Leu Asn Trp Ile Lys Ala Thr Ile Lys Ser Glu Ser Gly Phe
545                 550                 555                 560
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<210> 96
<211> 2124
<212> DNA
<213> Homo sapiens

<400> 96
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tccagccagt gctgaccagg gacttctgac ctgctggcca gccaggacct gtgtggggag 180
gccctcctgc tgccttgggg tgacaatctc agctccaggc tacagggaga ccgggaggat 240
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<210> 97
<211> 437
<212> PRT
<213> Homo sapiens

<400> 97
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Met Leu Gln Asp Pro Asp Ser Asp Gln Pro Leu Asn Ser Leu Asp Val
 1               5                  10                  15
Lys Pro Leu Arg Lys Pro Arg Ile Pro Met Glu Thr Phe Arg Lys Val
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                20                  25                  30
Gly Ile Pro Ile Ile Ile Ala Leu Leu Ser Leu Ala Ser Ile Ile Ile
        35                  40                  45
Val Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys
    50                  55                  60
Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu
65                  70                  75                  80
Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe
                85                  90                  95
Pro Glu Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr
            100                 105                 110
Leu Gln Val Leu Asp Ser Ala Thr Gly Asn Trp Phe Ser Ala Cys Phe
        115                 120                 125
Asp Asn Phe Thr Glu Ala Leu Ala Glu Thr Ala Cys Arg Gln Met Gly
    130                 135                 140
Tyr Ser Ser Lys Pro Thr Phe Arg Ala Val Glu Ile Gly Pro Asp Gln
145                 150                 155                 160
Asp Leu Asp Val Val Glu Ile Thr Glu Asn Ser Gln Glu Leu Arg Met
                165                 170                 175
Arg Asn Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His
            180                 185                 190
Cys Leu Ala Cys Gly Lys Ser Leu Lys Thr Pro Arg Val Val Gly Gly
        195                 200                 205
Glu Glu Ala Ser Val Asp Ser Trp Pro Trp Gln Val Ser Ile Gln Tyr
    210                 215                 220
Asp Lys Gln His Val Cys Gly Gly Ser Ile Leu Asp Pro His Trp Val
225                 230                 235                 240
Leu Thr Ala Ala His Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp
                245                 250                 255
Lys Val Arg Ala Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala
            260                 265                 270
Val Ala Lys Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp
        275                 280                 285
Asn Asp Ile Ala Leu Met Lys Leu Gln Phe Pro Leu Thr Phe Ser Gly
    290                 295                 300
Thr Val Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro
305                 310                 315                 320
Ala Thr Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn Gly
                325                 330                 335
Gly Lys Met Ser Asp Ile Leu Leu Gln Ala Ser Val Gln Val Ile Asp
            340                 345                 350
Ser Thr Arg Cys Asn Ala Asp Asp Ala Tyr Gln Gly Glu Val Thr Glu
        355                 360                 365
Lys Met Met Cys Ala Gly Ile Pro Glu Gly Gly Val Asp Thr Cys Gln
    370                 375                 380
Gly Asp Ser Gly Gly Pro Leu Met Tyr Gln Ser Asp Gln Trp His Val
385                 390                 395                 400
Val Gly Ile Val Ser Trp Gly Tyr Gly Cys Gly Gly Pro Ser Thr Pro
                405                 410                 415
Gly Val Tyr Thr Lys Val Ser Ala Tyr Leu Asn Trp Ile Tyr Asn Val
            420                 425                 430
Trp Lys Ala Glu Leu
        435
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<210> 98
<211> 1983
<212> DNA

<213> Homo sapiens

<400> 98
aatcaagctg cccaaagtcc cccaatcact cctggaatac acagagagag gcagcagctt 60
gctcagcgga caaggatgct gggcgtgagg gaccaaggcc tgccctgcac tcgggcctcc 120
tccagccagt gctgaccagg gacttctgac ctgctggcca gccaggacct gtgtggggag 180
gccctcctgc tgccttgggg tgacaatctc agctccaggc tacagggaga ccgggaggat 240
cacagagcca gcatggatcc tgacagtgat caacctctga acagcctcga tgtcaaaccc 300
ctgcgcaaac cccgtatccc catggagacc ttcagaaagg tggggatccc catcatcata 360
gcactactga gcctggcgag tatcatcatt gtggttgtcc tcatcaaggt gattctggat 420
aaatactact tcctctgcgg gcagcctctc cacttcatcc cgaggaagca gctgtgtgac 480
ggagagctgg actgtccctt gggggaggac gaggagcact gtgtcaagag cttccccgaa 540
gggcctgcag tggcagtccg cctctccaag gaccgatcca cactgcaggt gctggactcg 600
gccacaggga actggttctc tgcctgtttc gacaacttca cagaagctct cgctgagaca 660
gcctgtaggc agatgggcta cagcagcaaa cccactttca gagctgtgga gattggccca 720
gaccaggatc tggatgttgt tgaaatcaca gaaaacagcc aggagcttcg catgcggaac 780
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caggtcagca tccagtacga caaacagcac gtctgtggag ggagcatcct ggacccccac 960
tgggtcctca cggcagccca ctgcttcagg aaacataccg atgtgttcaa ctggaaggtg 1020
cgggcaggct cagacaaact gggcagcttc ccatccctgg ctgtggccaa gatcatcatc 1080
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caactggatc tacaatgtct ggaaggctga gctgtaatgc tgctgcccct ttgcagtgct 1440
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agagtccccc tgggtacacc cctctgccca cagcctcagc atttcttgga gcagcaaagg 1560
gcctcaattc ctgtaagaga ccctcgcagc ccagaggcgc ccagaggaag tcagcagccc 1620
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gtctcagggg tattgctaag ccaagaagga actttcccac actactgaat ggaagcaggc 1740
tgtcttgtaa aagcccagat cactgtgggc tggagaggag aaggaaaggg tctgcgccag 1800
ccctgtccgt cttcacccat ccccaagcct actagagcaa gaaaccagtt gtaatataaa 1860
atgcactgcc ctactgttgg tatgactacc gttacctact gttgtcattg ttattacagc 1920
tatggccact attattaaag agctgtgtaa catctctgga aaaaaaaaaa aaaaaaaaaa 1980
aaa 1983

<210> 99
<211> 335
<212> PRT
<213> Homo sapiens

<400> 99
Met Asp Pro Asp Ser Asp Gln Pro Leu Asn Ser Leu Asp Val Lys Pro
1 5 10 15
Leu Arg Lys Pro Arg Ile Pro Met Glu Thr Phe Arg Lys Val Gly Ile
20 25 30
Pro Ile Ile Ile Ala Leu Leu Ser Leu Ala Ser Ile Ile Ile Val Val
35 40 45
Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys Gly Gln
50 55 60
Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu Leu Asp
65 70 75 80
Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe Pro Glu
85 90 95
Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr Leu Gln
100 105 110

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Val Leu Asp Ser Ala Thr Gly Asn Trp Phe Ser Ala Cys Phe Asp Asn
        115                 120                 125
Phe Thr Glu Ala Leu Ala Glu Thr Ala Cys Arg Gln Met Gly Tyr Ser
    130                 135                 140
Ser Lys Pro Thr Phe Arg Ala Val Glu Ile Gly Pro Asp Gln Asp Leu
145                 150                 155                 160
Asp Val Val Glu Ile Thr Glu Asn Ser Gln Glu Leu Arg Met Arg Asn
                165                 170                 175
Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His Cys Leu
            180                 185                 190
Ala Cys Gly Lys Ser Leu Lys Thr Pro Arg Val Val Gly Gly Glu Glu
        195                 200                 205
Ala Ser Val Asp Ser Trp Pro Trp Gln Val Ser Ile Gln Tyr Asp Lys
    210                 215                 220
Gln His Val Cys Gly Gly Ser Ile Leu Asp Pro His Trp Val Leu Thr
225                 230                 235                 240
Ala Ala His Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp Lys Val
                245                 250                 255
Arg Ala Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala Val Ala
            260                 265                 270
Lys Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp Asn Asp
        275                 280                 285
Ile Ala Leu Met Lys Leu Gln Phe Pro Leu Thr Phe Ser Gly Thr Val
    290                 295                 300
Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro Ala Thr
305                 310                 315                 320
Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn Gly Gly
                325                 330                 335
```

<210> 100
<211> 855
<212> DNA
<213> Homo sapiens

<400> 100

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gtcctggcga gcccggccta cgtggccccc gccccaggcc aggccctgca gcaaacgggc 120
attgttgggg ggcaggaggc ccccaggagc aagtggccct ggcaggtgag cctgagagtc 180
cgcggcccat actggatgca cttctgcggg ggctccctca tccacccccа gtgggtgcta 240
accgcggcgc actgcgtgga accggacatc aaggatctgg ccgccctcag ggtgcaactg 300
cgggagcagc acctctacta ccaggaccag ctgctgccgg tcagcaggat catcgtgcac 360
ccacagttct acatcatcca gaccggggcg gacatcgccc tgctggagct ggaggagccc 420
gtgaacatct ccagccacat ccacacggtc acgctgcccc ctgcctcgga gaccttcccc 480
ccggggatgc cgtgctgggt cactggctgg ggcgacgtgg acaataatgt gcacctgccg 540
ccgccatacc cgctgaagga ggtggaagtc cccgtagtgg aaaaccacct ttgcaacgcg 600
gaatatcaca ccggcctcca tacgggccac agctttcaaa tcgtccgcga tgacatgctg 660
tgtgcgggga gcgaaaatca cgactcctgc cagggtgact ctggagggcc cctggtctgc 720
aaggtgaatg gcacctaact gcaggcgggc gtggtcagct gggaggagag ctgtgcccag 780
cccaaccggc ctggcatcta cacccgtgtc acctactact tggactggat ccaccactat 840
gtccccaaga agccc                                                  855
```

<210> 101
<211> 242
<212> PRT
<213> Homo sapiens

<400> 101

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Met Leu Leu Leu Ala Pro Gln Met Leu Ser Leu Leu Leu Leu Ala Leu
 1               5                  10                  15
Pro Val Leu Ala Ser Pro Ala Tyr Val Ala Pro Ala Pro Gly Gln Ala
            20                  25                  30
Leu Gln Gln Thr Gly Ile Val Gly Gly Gln Glu Ala Pro Arg Ser Lys
        35                  40                  45
Trp Pro Trp Gln Val Ser Leu Arg Val Arg Gly Pro Tyr Trp Met His
    50                  55                  60
Phe Cys Gly Gly Ser Leu Ile His Pro Gln Trp Val Leu Thr Ala Ala
65                  70                  75                  80
His Cys Val Glu Pro Asp Ile Lys Asp Leu Ala Ala Leu Arg Val Gln
                85                  90                  95
Leu Arg Glu Gln His Leu Tyr Tyr Gln Asp Gln Leu Leu Pro Val Ser
            100                 105                 110
Arg Ile Ile Val His Pro Gln Phe Tyr Ile Ile Gln Thr Gly Ala Asp
        115                 120                 125
Ile Ala Leu Leu Glu Leu Glu Glu Pro Val Asn Ile Ser Ser His Ile
    130                 135                 140
His Thr Val Thr Leu Pro Pro Ala Ser Glu Thr Phe Pro Pro Gly Met
145                 150                 155                 160
Pro Cys Trp Val Thr Gly Trp Gly Asp Val Asp Asn Asn Val His Leu
                165                 170                 175
Pro Pro Pro Tyr Pro Leu Lys Glu Val Glu Val Pro Val Val Glu Asn
            180                 185                 190
His Leu Cys Asn Ala Glu Tyr His Thr Gly Leu His Thr Gly His Ser
        195                 200                 205
Phe Gln Ile Val Arg Asp Asp Met Leu Cys Ala Gly Ser Glu Asn His
    210                 215                 220
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Val Asn
225                 230                 235                 240
Gly Thr
```

<210> 102
<211> 1462
<212> DNA
<213> Homo sapiens

<400> 102

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ctgtctcaaa aaattaaaaa aaataataat aataataatg aatgaagctg gacggacttc 60
gcgtgcaccg cggtcagctc ggggtctgct ggggggtctg ggtcagctca gggtccagga 120
accgaggcca acggcacccc gtgctgcgct ggggtgaggg gtctgccctg gggtctcggg 180
gttcagggct aggtcacgga ggagtcggct ctgggcgctt ccttcctgag gagaggagct 240
gggcaggccg ggccgacggg ttgggccgca tagccgggcc tgtgctcatc tccagcataa 300
aactccactt catggagcct gcacctcgct cgtgctccaa cgcttctgcc accgccgacc 360
acggccctgc gccccagcca ggcctgagga catgaggcgg ccggcggcgg tgccgctcct 420
gctgctgctg tgttttgggt ctcagagggc caaggcagca acagcctgtg gtcgccccag 480
gatgctgaac cgaatggtgg gcgggcagga cacgcaggag ggcgagtggc cctggcaagt 540
cagcatccag cgcaacggaa gccacttctg cgggggcagc ctcatcgcgg agcagtgggt 600
cctgacggct gcgcactgct tccgcaacac ctctgagacg tccctgtacc aggtcctgct 660
gggggcaagg cagctagtgc agccgggacc acacgctatg tatgcccggg tgaggcaggt 720
ggagagcaac cccctgtacc agggcacggc ctccagcgct gacgtggccc tggtggagct 780
ggaggcacca gtgcccttca ccaattacat cctccccgtg tgcctgcctg acccctcggt 840
gatctttgag acgggcatga actgctgggt cactggctgg ggcagcccca gtgaggaaga 900
cctcctgccc gaaccgcgga tcctgcagaa actcgctgtg cccatcatcg acacacccaa 960
gtgcaacctg ctctacagca aagacaccga gtttggctac caacccaaaa ccatcaagaa 1020
tgacatgctg tgcgccggct tcgaggaggg caagaaggat gcctgcaagg gcgactcggg 1080
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cggcccccctg gtgtgcctcg tgggtcagtc gtggctgcag gcgggggtga tcagctgggg 1140
tgagggctgt gcccgccaga accgcccagg tgtctacatc cgtgtcaccg cccaccacaa 1200
ctggatccat cggatcatcc ccaaactgca gttccagcca gcgaggttgg gcggccagaa 1260
gtgagacccc cggggccagg agccccttga gcagagctct gcacccagcc tgcccgccca 1320
caccatcctg ctggtcctcc cagcgctgct gttgcacctg tgagccccac cagactcatt 1380
tgtaaatagc gctccttcct cccctctcaa atacccttat tttatttatg tttctcccaa 1440
taaaaaccca gcctgtgtgc ca 1462

<210> 103
<211> 290
<212> PRT
<213> Homo sapiens

<400> 103
Met Arg Arg Pro Ala Ala Val Pro Leu Leu Leu Leu Leu Cys Phe Gly
1 5 10 15
Ser Gln Arg Ala Lys Ala Ala Thr Ala Cys Gly Arg Pro Arg Met Leu
20 25 30
Asn Arg Met Val Gly Gly Gln Asp Thr Gln Glu Gly Glu Trp Pro Trp
35 40 45
Gln Val Ser Ile Gln Arg Asn Gly Ser His Phe Cys Gly Gly Ser Leu
50 55 60
Ile Ala Glu Gln Trp Val Leu Thr Ala Ala His Cys Phe Arg Asn Thr
65 70 75 80
Ser Glu Thr Ser Leu Tyr Gln Val Leu Leu Gly Ala Arg Gln Leu Val
85 90 95
Gln Pro Gly Pro His Ala Met Tyr Ala Arg Val Arg Gln Val Glu Ser
100 105 110
Asn Pro Leu Tyr Gln Gly Thr Ala Ser Ser Ala Asp Val Ala Leu Val
115 120 125
Glu Leu Glu Ala Pro Val Pro Phe Thr Asn Tyr Ile Leu Pro Val Cys
130 135 140
Leu Pro Asp Pro Ser Val Ile Phe Glu Thr Gly Met Asn Cys Trp Val
145 150 155 160
Thr Gly Trp Gly Ser Pro Ser Glu Glu Asp Leu Leu Pro Glu Pro Arg
165 170 175
Ile Leu Gln Lys Leu Ala Val Pro Ile Ile Asp Thr Pro Lys Cys Asn
180 185 190
Leu Leu Tyr Ser Lys Asp Thr Glu Phe Gly Tyr Gln Pro Lys Thr Ile
195 200 205
Lys Asn Asp Met Leu Cys Ala Gly Phe Glu Glu Gly Lys Lys Asp Ala
210 215 220
Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Val Gly Gln Ser
225 230 235 240
Trp Leu Gln Ala Gly Val Ile Ser Trp Gly Glu Gly Cys Ala Arg Gln
245 250 255
Asn Arg Pro Gly Val Tyr Ile Arg Val Thr Ala His His Asn Trp Ile
260 265 270
His Arg Ile Ile Pro Lys Leu Gln Phe Gln Pro Ala Arg Leu Gly Gly
275 280 285
Gln Lys
290

<210> 104
<211> 1755
<212> DNA
<213> Homo sapiens

<400> 104
ccaggacttc cgtctgagat gggatttctg gacagaacaa tggagcgcag aagctccagc 60
aacgtgtgct ctgcagggag cccagaccag agtccaagcc ctaggcagtg ccacccttac 120
ccagcccagc cttgaagaca gaatgagagg ggtttcctgt ctccaggtcc tgctccttct 180
ggtgctggga gctgctggga ctcagggaag gaagtctgca gcctgcgggc agccccgcat 240
gtccagtcgg atcgttgggg gccgggatgg ccgggacgga gagtggccgt ggcaggcgag 300
catccagcat cgtggggcac acgtgtgcgg ggggtcgctc atcgcccccc agtgggtgct 360
gacagcggcg cactgcttcc ccaggagggc actgccagct gagtaccgcg tgcgcctggg 420
ggcgctgcgt ctgggctcca cctcgccccg cacgctctcg gtgcccgtgc gacgggtgct 480
gctgcccccg gactactccg aggacggggc ccgcggcgac ctggcactgc tgcagctgcg 540
tcgcccggtg cccctgagcg ctcgcgtcca acccgtctgc ctgcccgtgc ccggcgcccg 600
cccgccgccc ggcacaccat gccgggtcac cggctggggc agcctccgcc caggagtgcc 660
cctcccagag tggcgaccgc tacaaggagt aagggtgccg ctgctggact cgcgcacctg 720
cgacggcctc taccacgtgg gcgcggacgt gccccaggct gagcgcattg tgctgcctgg 780
gagtctgtgt gccggctacc cccagggcca caaggacgcc tgccagggtg attctggggg 840
acctctgacc tgcctgcagt ctgggagctg ggtcctggtg ggcgtggtga gctggggcaa 900
gggttgtgcc ctgcccaacc gtccaggggt ctacaccagt gtggccacat atagcccctg 960
gattcaggct cgcgtcagct tctaatgcta gccggtgagg ctgacctgga gccagctgct 1020
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tcgaggccaa gatgcctaaa aaagctaaag gccaccccac cccccaccca ccacctcctg 1140
cctcctctcc tctttgggga tcaccagctc tgactccacc aaccctcatc caggaatctg 1200
ccatgagtcc cagggagtca cactccccac tcccttcctg gcttgtattt acttttcttg 1260
gccctggcca gggctgggcg caaggcacgc agtgatgggc aaaccaattg ctgcccatct 1320
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accagggaga tcctccatag ctggctttga ggacacgggg accacagcca tgagcggcct 1440
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ctgagccact cctgacctac aaagttgtga cttaataaat gtgtgctttg aacccaaaaa 1680
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740
aaaaaaaaaa aaaaa 1755

<210> 105
<211> 284
<212> PRT
<213> Homo sapiens

<400> 105
Met Arg Gly Val Ser Cys Leu Gln Val Leu Leu Leu Leu Val Leu Gly
 1   5   10   15
Ala Ala Gly Thr Gln Gly Arg Lys Ser Ala Ala Cys Gly Gln Pro Arg
            20   25   30
Met Ser Ser Arg Ile Val Gly Gly Arg Asp Gly Arg Asp Gly Glu Trp
        35   40   45
Pro Trp Gln Ala Ser Ile Gln His Pro Gly Ala His Val Cys Gly Gly
    50   55   60
Ser Leu Ile Ala Pro Gln Trp Val Leu Thr Ala Ala His Cys Phe Pro
65   70   75   80
Arg Arg Ala Leu Pro Ala Glu Tyr Arg Val Arg Leu Gly Ala Leu Arg
                85   90   95
Leu Gly Ser Thr Ser Pro Arg Thr Leu Ser Val Pro Val Arg Arg Val
            100   105   110
Leu Leu Pro Pro Asp Tyr Ser Glu Asp Gly Ala Arg Gly Asp Leu Ala
        115   120   125
Leu Leu Gln Leu Arg Arg Pro Val Pro Leu Ser Ala Arg Val Gln Pro
    130   135   140
Val Cys Leu Pro Val Pro Gly Ala Arg Pro Pro Pro Gly Thr Pro Cys

```
145                 150                 155                 160
Arg Val Thr Gly Trp Gly Ser Leu Arg Pro Gly Val Pro Leu Pro Glu
                165                 170                 175
Trp Arg Pro Leu Gln Gly Val Arg Val Pro Leu Leu Asp Ser Arg Thr
            180                 185                 190
Cys Asp Gly Leu Tyr His Val Gly Ala Asp Val Pro Gln Ala Glu Arg
        195                 200                 205
Ile Val Leu Pro Gly Ser Leu Cys Ala Gly Tyr Pro Gln Gly His Lys
    210                 215                 220
Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Thr Cys Leu Gln Ser
225                 230                 235                 240
Gly Ser Trp Val Leu Val Gly Val Val Ser Trp Gly Lys Gly Cys Ala
                245                 250                 255
Leu Pro Asn Arg Pro Gly Val Tyr Thr Ser Val Ala Thr Tyr Ser Pro
            260                 265                 270
Trp Ile Gln Ala Arg Val Thr Ser Asn Ala Ser Arg
        275                 280
```

<210> 106
<211> 321
<212> DNA
<213> Homo sapiens

<400> 106
gcgctggtgg cgggcggagt ggagtccgcg cgcgggcgct ggccatggca ggccagcctg 60
cgcctgagga gacgccaccg atgtggaggg agcctgctca gccgccgctg ggtgctctcg 120
gctgcgcact gcttcgctcc ccagggtgac tcaggtggac ccttggtctg tgacaaggat 180
ggactgtggt atcaggttgg aatcgtgagc tggggaatgg actgcggtca acccaatcgg 240
cctggtgtct acaccaacat cagtgtgtac ttccactgga tccggagggt gatgtcccac 300
agtacaccca ggccaaaccc c 321

<210> 107
<211> 107
<212> PRT
<213> Homo sapiens

<400> 107
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Ala Leu Val Ala Gly Gly Val Glu Ser Ala Arg Gly Arg Trp Pro Trp
 1               5                  10                  15
Gln Ala Ser Leu Arg Leu Arg Arg Arg His Arg Cys Gly Gly Ser Leu
            20                  25                  30
Leu Ser Arg Arg Trp Val Leu Ser Ala Ala His Cys Phe Ala Pro Gln
        35                  40                  45
Gly Asp Ser Gly Gly Pro Leu Val Cys Asp Lys Asp Gly Leu Trp Tyr
    50                  55                  60
Gln Val Gly Ile Val Ser Trp Gly Met Asp Cys Gly Gln Pro Asn Arg
65                  70                  75                  80
Pro Gly Val Tyr Thr Asn Ile Ser Val Tyr Phe His Trp Ile Arg Arg
                85                  90                  95
Val Met Ser His Ser Thr Pro Arg Pro Asn Pro
            100                 105
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<210> 108
<211> 2468
<212> DNA
<213> Homo sapiens

<400> 108
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ggaaagggct gtgtttatgg gaagccagta acactgtggc ctactatctc ttccgtggtg 120
ccatctacat ttttgggact cgggaattat gaggtagagg tggaggcgga gccggatgtc 180
agaggtcctg aaatagtcac catgggggaa aatgatccgc ctgctgttga agcccccttc 240
tcattccgat cgcttttttgg ccttgatgat ttgaaaataa gtcctgttgc accagatgca 300
gatgctgttg ctgcacagat cctgtcactg ctgccattga agtttttttcc aatcatcgtc 360
attgggatca ttgcattgat attagcactg gccattggtc tgggcatcca cttcgactgc 420
tcagggaagt acagatgtcg ctcatccttt aagtgtatcg agctgatagc tcgatgtgac 480
ggagtctcgg attgcaaaga cggggaggac gagtaccgct gtgtccgggt gggtggtcag 540
aatgccgtgc tccaggtgtt cacagctgct tcgtggaaga ccatgtgctc cgatgactgg 600
aagggtcact acgcaaatgt tgcctgtgcc caactgggtt tcccaagcta tgtgagttca 660
gataacctca gagtgagctc gctggagggg cagttccggg aggagtttgt gtccatcgat 720
cacctcttgc cagatgacaa ggtgactgca ttacaccact cagtatatgt gagggaggga 780
tgtgcctctg gccacgtggt taccttgcag tgcacagcct gtggtcatag aaggggctac 840
agctcacgca tcgtgggtgg aaacatgtcc ttgctctcgc agtggccctg gcaggccagc 900
cttcagttcc agggctacca cctgtgcggg ggctctgtca tcacgccccc gtggatcatc 960
actgctgcac actgtgttta tgacttgtac ctccccaagt catggaccat ccaggtgggt 1020
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gatggaaaag tgtgctggac gtcaggatgg ggggccacag aggatggagc aggtgacgcc 1260
tcccctgtcc tgaaccacgc ggccgtccct ttgatttcca acaagatctg caaccacagg 1320
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aagttagtgg gagcgaccag ctttggcatc ggctgcgcag aggtgaacaa gcctggggtg 1500
tacacccgtg tcacctcctt cctggactgg atccacgagc agatggagag agacctaaaa 1560
acctgaagag gaaggggaca agtagccacc tgagttcctg aggtgatgaa gacagcccga 1620
tcctcccctg gactcccgtg taggaacctg cacacgagca gacacccttg gagctctgag 1680
ttccggcacc agtagcaggc ccgaaagagg cacccttcca tctgattcca gcacaacctt 1740
caagctgctt tttgtttttt gttttttga ggtggagtct cgctctgttg cccaggctgg 1800
agtgcagtgg cgaaatccct gctcactgca gcctccgctt ccctggttca agcgattctc 1860
ttgcctcagc ttccccagta gctgggacca caggtgcccg ccaccacacc caactaattt 1920
ttgtattttt agtagagaca gggtttcacc atgttggcca ggctgctctc aaaccctga 1980
cctcaaatga tgtgcctgct tcagcctccc acagtgctgg gattacaggc atgggccacc 2040
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agggcggcct ttcccactgg tccatctggt tttctctcca ggggtcttgc aaaattcctg 2160
acgagataag cagttatgtg acctcacgtg caaagccacc aacagccact cagaaaagac 2220
gcaccagccc agaagtgcag aactgcagtc actgcacgtt ttcatctcta gggaccagaa 2280
ccaaacccac cctttctact tccaagactt attttcacat gtggggaggt taatctagga 2340
atgactcgtt taaggcctat tttcatgatt tctttgtagc atttggtgct tgacgtatta 2400
ttgtcctttg attccaaata atatgtttcc ttccctcaaa aaaaaaaaaa aaaaaaaaaa 2460
aaaaaaaa 2468

<210> 109
<211> 454
<212> PRT
<213> Homo sapiens

<400> 109
Met Gly Glu Asn Asp Pro Pro Ala Val Glu Ala Pro Phe Ser Phe Arg
 1   5   10   15
Ser Leu Phe Gly Leu Asp Asp Leu Lys Ile Ser Pro Val Ala Pro Asp
            20   25   30
Ala Asp Ala Val Ala Ala Gln Ile Leu Ser Leu Leu Pro Leu Lys Phe
        35   40   45
Phe Pro Ile Ile Val Ile Gly Ile Ile Ala Leu Ile Leu Ala Leu Ala

```
    50                  55                  60
Ile Gly Leu Gly Ile His Phe Asp Cys Ser Gly Lys Tyr Arg Cys Arg
65                  70                  75                  80
Ser Ser Phe Lys Cys Ile Glu Leu Ile Ala Arg Cys Asp Gly Val Ser
                85                  90                  95
Asp Cys Lys Asp Gly Glu Asp Glu Tyr Arg Cys Val Arg Val Gly Gly
            100                 105                 110
Gln Asn Ala Val Leu Gln Val Phe Thr Ala Ala Ser Trp Lys Thr Met
        115                 120                 125
Cys Ser Asp Asp Trp Lys Gly His Tyr Ala Asn Val Ala Cys Ala Gln
    130                 135                 140
Leu Gly Phe Pro Ser Tyr Val Ser Ser Asp Asn Leu Arg Val Ser Ser
145                 150                 155                 160
Leu Glu Gly Gln Phe Arg Glu Glu Phe Val Ser Ile Asp His Leu Leu
                165                 170                 175
Pro Asp Asp Lys Val Thr Ala Leu His His Ser Val Tyr Val Arg Glu
            180                 185                 190
Gly Cys Ala Ser Gly His Val Val Thr Leu Gln Cys Thr Ala Cys Gly
        195                 200                 205
His Arg Arg Gly Tyr Ser Ser Arg Ile Val Gly Gly Asn Met Ser Leu
    210                 215                 220
Leu Ser Gln Trp Pro Trp Gln Ala Ser Leu Gln Phe Gln Gly Tyr His
225                 230                 235                 240
Leu Cys Gly Gly Ser Val Ile Thr Pro Leu Trp Ile Ile Thr Ala Ala
                245                 250                 255
His Cys Val Tyr Asp Leu Tyr Leu Pro Lys Ser Trp Thr Ile Gln Val
            260                 265                 270
Gly Leu Val Ser Leu Leu Asp Asn Pro Ala Pro Ser His Leu Val Glu
        275                 280                 285
Lys Ile Val Tyr His Ser Lys Tyr Lys Pro Lys Arg Leu Gly Asn Asp
    290                 295                 300
Ile Ala Leu Met Lys Leu Ala Gly Pro Leu Thr Phe Asn Glu Met Ile
305                 310                 315                 320
Gln Pro Val Cys Leu Pro Asn Ser Glu Glu Asn Phe Pro Asp Gly Lys
                325                 330                 335
Val Cys Trp Thr Ser Gly Trp Gly Ala Thr Glu Asp Gly Ala Gly Asp
            340                 345                 350
Ala Ser Pro Val Leu Asn His Ala Ala Val Pro Leu Ile Ser Asn Lys
        355                 360                 365
Ile Cys Asn His Arg Asp Val Tyr Gly Gly Ile Ile Ser Pro Ser Met
    370                 375                 380
Leu Cys Ala Gly Tyr Leu Thr Gly Gly Val Asp Ser Cys Gln Gly Asp
385                 390                 395                 400
Ser Gly Gly Pro Leu Val Cys Gln Glu Arg Arg Leu Trp Lys Leu Val
                405                 410                 415
Gly Ala Thr Ser Phe Gly Ile Gly Cys Ala Glu Val Asn Lys Pro Gly
            420                 425                 430
Val Tyr Thr Arg Val Thr Ser Phe Leu Asp Trp Ile His Glu Gln Met
        435                 440                 445
Glu Arg Asp Leu Lys Thr
    450
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<210> 110
<211> 2554
<212> DNA
<213> Homo sapiens

<400> 110
gccacgttgg attagggccc accctaatga ctcattttaa ctagatgact ctgtaaagac 60
tctccaggcc atctccaaat aagatgccat tctgaggtac taagagttaa gacctcaacg 120
tgtctttctg ggggatacta ttcaacccat agcacatccc ctcatccccc atggaataac 180
cgggtcagag gtggagcagg taggactgaa ctagagaatg tgccccttgg tgggtggccc 240
tttccctaat taaggcacct ttctttgggc tgagacttct ctgcaaagag gggaggggga 300
aaggatagtt aaatttgtaa gtttcatggc actccaagtc aggttctggg gctttctgct 360
cttccttttt ctggttatca gatgcagatg ctgttgctgc acagatcctg tcactgctgc 420
cattgaagtt ttttccaatc atcgtcattg ggatcattgc attgatatta gcactggcca 480
ttggtctggg catccacttc gactgctcag ggaagtacag atgtcgctca tcctttaagt 540
gtatcgagct gatagctcga tgtgacggag tctcggattg caaagacggg gaggacgagt 600
accgctgtgt ccgggtgggt ggtcagaatg ccgtgctcca ggtgttcaca gctgcttcgt 660
ggaagaccat gtgctccgat gactggaagg gtcactacgc aaatgttgcc tgtgcccaac 720
tgggtttccc aagctatgtg agttcagata acctcagagt gagctcgctg gaggggcagt 780
tccgggagga gtttgtgtcc atcgatcacc tcttgccaga tgacaaggtg actgcattac 840
accactcagt atatgtgagg gagggatgtg cctctggcca cgtggttacc ttgcagtgca 900
cagcctgtgg tcatagaagg ggctacagct cacgcatcgt gggtggaaac atgtccttgc 960
tctcgcagtg gccctggcag gccagccttc agttccaggg ctaccacctg tgcgggggct 1020
ctgtcatcac gcccctgtgg atcatcactg ctgcacactg tgtttatgac ttgtacctcc 1080
ccaagtcatg gaccatccag gtgggtctag tttccctgtt ggacaatcca gccccatccc 1140
acttggtgga gaagattgtc taccacagca agtacaagcc aaagaggctg ggcaatgaca 1200
tcgcccttat gaagctggcc gggccactca cgttcaatga aatgatccag cctgtgtgcc 1260
tgcccaactc tgaagagaac ttccccgatg gaaaagtgtg ctggacgtca ggatgggggg 1320
ccacagagga tggagcaggt gacgcctccc ctgtcctgaa ccacgcggcc gtccctttga 1380
tttccaacaa gatctgcaac cacagggacg tgtacggtgg catcatctcc ccctccatgc 1440
tctgcgcggg ctacctgacg ggtggcgtgg acagctgcca gggggacagc ggggggcccc 1500
tggtgtgtca agagaggagg ctgtggaagt tagtgggagc gaccagcttt ggcatcggct 1560
gcgcagaggt gaacaagcct ggggtgtaca cccgtgtcac ctccttcctg gactggatcc 1620
acgagcagat ggagagagac ctaaaaacct gaagaggaag gggacaagta gccacctgag 1680
ttcctgaggt gatgaagaca gcccgatcct cccctggact cccgtgtagg aacctgcaca 1740
cgagcagaca cccttggagc tctgagttcc ggcaccagta gcaggcccga aagaggcacc 1800
cttccatctg attccagcac aaccttcaag ctgctttttg ttttttgttt ttttgaggtg 1860
gagtctcgct ctgttgccca ggctggagtg cagtggcgaa atccctgctc actgcagcct 1920
ccgcttccct ggttcaagcg attctcttgc ctcagcttcc ccagtagctg ggaccacagg 1980
tgcccgccac cacacccaac taatttttgt atttttagta gagacagggt ttcaccatgt 2040
tggccaggct gctctcaaac ccctgacctc aaatgatgtg cctgcttcag cctcccacag 2100
tgctgggatt acaggcatgg gccaccacgc ctagcctcac gctccttttct gatcttcact 2160
aagaacaaaa gaagcagcaa cttgcaaggg cggcctttcc cactggtcca tctggttttc 2220
tctccagggg tcttgcaaaa ttcctgacga gataagcagt tatgtgacct cacgtgcaaa 2280
gccaccaaca gccactcaga aaagacgcac cagcccagaa gtgcagaact gcagtcactg 2340
cacgttttca tctctaggga ccagaaccaa acccaccctt tctacttcca agacttattt 2400
tcacatgtgg ggaggttaat ctaggaatga ctcgtttaag gcctattttc atgatttctt 2460
tgtagcattt ggtgcttgac gtattattgt cctttgattc caaataatat gtttccttcc 2520
ctcaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 2554

<210> 111
<211> 327
<212> PRT
<213> Homo sapiens

<400> 111
Met Cys Ser Asp Asp Trp Lys Gly His Tyr Ala Asn Val Ala Cys Ala
 1   5   10   15
Gln Leu Gly Phe Pro Ser Tyr Val Ser Ser Asp Asn Leu Arg Val Ser
            20   25   30
Ser Leu Glu Gly Gln Phe Arg Glu Glu Phe Val Ser Ile Asp His Leu
        35   40   45
Leu Pro Asp Asp Lys Val Thr Ala Leu His His Ser Val Tyr Val Arg

```
    50                  55                  60
Glu Gly Cys Ala Ser Gly His Val Val Thr Leu Gln Cys Thr Ala Cys
65                  70                  75                  80
Gly His Arg Arg Gly Tyr Ser Ser Arg Ile Val Gly Gly Asn Met Ser
                85                  90                  95
Leu Leu Ser Gln Trp Pro Trp Gln Ala Ser Leu Gln Phe Gln Gly Tyr
            100                 105                 110
His Leu Cys Gly Gly Ser Val Ile Thr Pro Leu Trp Ile Ile Thr Ala
        115                 120                 125
Ala His Cys Val Tyr Asp Leu Tyr Leu Pro Lys Ser Trp Thr Ile Gln
    130                 135                 140
Val Gly Leu Val Ser Leu Leu Asp Asn Pro Ala Pro Ser His Leu Val
145                 150                 155                 160
Glu Lys Ile Val Tyr His Ser Lys Tyr Lys Pro Lys Arg Leu Gly Asn
                165                 170                 175
Asp Ile Ala Leu Met Lys Leu Ala Gly Pro Leu Thr Phe Asn Glu Met
            180                 185                 190
Ile Gln Pro Val Cys Leu Pro Asn Ser Glu Glu Asn Phe Pro Asp Gly
        195                 200                 205
Lys Val Cys Trp Thr Ser Gly Trp Gly Ala Thr Glu Asp Gly Ala Gly
    210                 215                 220
Asp Ala Ser Pro Val Leu Asn His Ala Ala Val Pro Leu Ile Ser Asn
225                 230                 235                 240
Lys Ile Cys Asn His Arg Asp Val Tyr Gly Gly Ile Ile Ser Pro Ser
                245                 250                 255
Met Leu Cys Ala Gly Tyr Leu Thr Gly Gly Val Asp Ser Cys Gln Gly
            260                 265                 270
Asp Ser Gly Gly Pro Leu Val Cys Gln Glu Arg Arg Leu Trp Lys Leu
        275                 280                 285
Val Gly Ala Thr Ser Phe Gly Ile Gly Cys Ala Glu Val Asn Lys Pro
    290                 295                 300
Gly Val Tyr Thr Arg Val Thr Ser Phe Leu Asp Trp Ile His Glu Gln
305                 310                 315                 320
Met Glu Arg Asp Leu Lys Thr
                325
```

<210> 112
<211> 2135
<212> DNA
<213> Homo sapiens

<400> 112

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gcagggggac agttgttagt gttgcactct gaaagagctg ttggttaatt cctgccttcc 60
tccctttttcc cagtccactt cgactgctca gggaagtaca gatgtcgctc atcctttaag 120
tgtatcgagc tgatagctcg atgtgacgga gtctcggatt gcaaagacgg ggaggacgag 180
taccgctgtg tccgggtggg tggtcagaat gccgtgctcc aggtgttcac agctgcttcg 240
tggaagacca tgtgctccga tgactggaag ggtcactacg caaatgttgc ctgtgcccaa 300
ctgggtttcc caagctatgt gagttcagat aacctcagag tgagctcgct ggaggggcag 360
ttccgggagg agtttgtgtc catcgatcac ctcttgccag atgacaaggt gactgcatta 420
caccactcag tatatgtgag ggagggatgt gcctctggcc acgtggttac cttgcagtgc 480
acagcctgtg gtcatagaag gggctacagc tcacgcatcg tgggtggaaa catgtccttg 540
ctctcgcagt ggccctggca ggccagcctt cagttccagg gctaccacct gtgcgggggc 600
tctgtcatca cgcccctgtg gatcatcact gctgcacact gtgtttatga cttgtacctc 660
cccaagtcat ggaccatcca ggtgggtcta gtttccctgt tggacaatcc agccccatcc 720
cacttggtgg agaagattgt ctaccacagc aagtacaagc caaagaggct gggcaatgac 780
atcgccctta tgaagctggc cgggccactc acgttcaatg aaatgatcca gcctgtgtgc 840
ctgcccaact ctgaagagaa cttccccgat ggaaaagtgt gctggacgtc aggatggggg 900
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gccacagagg atggagcagg tgacgcctcc cctgtcctga accacgcggc cgtccctttg 960
atttccaaca agatctgcaa ccacagggac gtgtacggtg gcatcatctc cccctccatg 1020
ctctgcgcgg gctacctgac gggtggcgtg gacagctgcc agggggacag cgggggccc 1080
ctggtgtgtc aagagaggag gctgtggaag ttagtgggag cgaccagctt tggcatcggc 1140
tgcgcagagg tgaacaagcc tggggtgtac acccgtgtca cctccttcct ggactggatc 1200
cacgagcaga tggagagaga cctaaaaacc tgaagaggaa ggggacaagt agccacctga 1260
gttcctgagg tgatgaagac agcccgatcc tcccctggac tcccgtgtag gaacctgcac 1320
acgagcagac acccttggag ctctgagttc cggcaccagt agcaggcccg aaagaggcac 1380
ccttccatct gattccagca caaccttcaa gctgcttttt gtttttgttt ttttgaggt 1440
ggagtctcgc tctgttgccc aggctggagt gcagtggcga aatccctgct cactgcagcc 1500
tccgcttccc tggttcaagc gattctcttg cctcagcttc cccagtagct gggaccacag 1560
gtgcccgcca ccacacccaa ctaatttttg tatttttagt agagacaggg tttcaccatg 1620
ttggccaggc tgctctcaaa ccctgacct caaatgatgt gcctgcttca gcctcccaca 1680
gtgctgggat tacaggcatg ggccaccacg cctagcctca cgctcctttc tgatcttcac 1740
taagaacaaa agaagcagca acttgcaagg gcggcctttc ccactggtcc atctggtttt 1800
ctctccaggg gtcttgcaaa attcctgacg agataagcag ttatgtgacc tcacgtgcaa 1860
agccaccaac agccactcag aaaagacgca ccagcccaga agtgcagaac tgcagtcact 1920
gcacgttttc atctctaggg accagaacca aacccaccct ttctacttcc aagacttatt 1980
ttcacatgtg gggaggttaa tctaggaatg actcgtttaa ggcctatttt catgatttct 2040
ttgtagcatt tggtgcttga cgtattattg tcctttgatt ccaaataata tgtttccttc 2100
cctcaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 2135

<210> 113
<211> 327
<212> PRT
<213> Homo sapiens

<400> 113
Met Cys Ser Asp Asp Trp Lys Gly His Tyr Ala Asn Val Ala Cys Ala
1 5 10 15
Gln Leu Gly Phe Pro Ser Tyr Val Ser Ser Asp Asn Leu Arg Val Ser
20 25 30
Ser Leu Glu Gly Gln Phe Arg Glu Glu Phe Val Ser Ile Asp His Leu
35 40 45
Leu Pro Asp Asp Lys Val Thr Ala Leu His His Ser Val Tyr Val Arg
50 55 60
Glu Gly Cys Ala Ser Gly His Val Val Thr Leu Gln Cys Thr Ala Cys
65 70 75 80
Gly His Arg Arg Gly Tyr Ser Ser Arg Ile Val Gly Gly Asn Met Ser
85 90 95
Leu Leu Ser Gln Trp Pro Trp Gln Ala Ser Leu Gln Phe Gln Gly Tyr
100 105 110
His Leu Cys Gly Gly Ser Val Ile Thr Pro Leu Trp Ile Ile Thr Ala
115 120 125
Ala His Cys Val Tyr Asp Leu Tyr Leu Pro Lys Ser Trp Thr Ile Gln
130 135 140
Val Gly Leu Val Ser Leu Leu Asp Asn Pro Ala Pro Ser His Leu Val
145 150 155 160
Glu Lys Ile Val Tyr His Ser Lys Tyr Lys Pro Lys Arg Leu Gly Asn
165 170 175
Asp Ile Ala Leu Met Lys Leu Ala Gly Pro Leu Thr Phe Asn Glu Met
180 185 190
Ile Gln Pro Val Cys Leu Pro Asn Ser Glu Glu Asn Phe Pro Asp Gly
195 200 205
Lys Val Cys Trp Thr Ser Gly Trp Gly Ala Thr Glu Asp Gly Ala Gly
210 215 220
Asp Ala Ser Pro Val Leu Asn His Ala Ala Val Pro Leu Ile Ser Asn
225 230 235 240

```
Lys Ile Cys Asn His Arg Asp Val Tyr Gly Gly Ile Ile Ser Pro Ser
                245                 250                 255
Met Leu Cys Ala Gly Tyr Leu Thr Gly Gly Val Asp Ser Cys Gln Gly
            260                 265                 270
Asp Ser Gly Gly Pro Leu Val Cys Gln Glu Arg Arg Leu Trp Lys Leu
        275                 280                 285
Val Gly Ala Thr Ser Phe Gly Ile Gly Cys Ala Glu Val Asn Lys Pro
    290                 295                 300
Gly Val Tyr Thr Arg Val Thr Ser Phe Leu Asp Trp Ile His Glu Gln
305                 310                 315                 320
Met Glu Arg Asp Leu Lys Thr
                325
```

<210> 114
<211> 1359
<212> DNA
<213> Homo sapiens

<400> 114
accgggcacc ggacggctcg ggtactttcg ttcttaatta ggtcatgccc gtgtgagcca 60
ggaaagggct gtgtttatgg gaagccagta acactgtggc ctactatctc ttccgtggtg 120
ccatctacat ttttgggact cgggaattat gaggtagagg tggaggcgga gccggatgtc 180
agaggtcctg aaatagtcac catgggggaa aatgatccgc ctgctgttga agcccccttc 240
tcattccgat cgcttttttgg ccttgatgat ttgaaaataa gtcctgttgc accagatgca 300
gatgctgttg ctgcacagat cctgtcactg ctgccattga agtttttcc aatcatcgtc 360
attgggatca ttgcattgat attagcactg gccattggtc tgggcatcca cttcgactgc 420
tcagggaagt acagatgtcg ctcatccttt aagtgtatcg agctgatagc tcgatgtgac 480
ggagtctcgg attgcaaaga cggggaggac gagtaccgct gtgtccgggt gggtggtcag 540
aatgccgtgc tccaggtgtt cacagctgct tcgtggaaga ccatgtgctc cgatgactgg 600
aagggtcact acgcaaatgt tgcctgtgcc caactgggtt tcccaagcta tgtgagttca 660
gataacctca gagtgagctc gctggagggg cagttccggg aggagtttgt gtccatcgat 720
cacctcttgc cagatgacaa ggtgactgca ttacaccact cagtatatgt gagggaggga 780
tgtgcctctg gccacgtggt taccttgcag tgcacagcct gtggtcatag aaggggctac 840
agctcacgca tcgtgggtgg aaacatgtcc ttgctctcgc agtggccctg gcaggccagc 900
cttcagttcc agggctacca cctgtgcggg ggctctgtca tcacgccccc gtggatcatc 960
actgctgcac actgtgttta tgacttgtac ctccccaagt catggaccat ccaggtgggt 1020
ctagtttccc tgttggacaa tccagcccca tcccacttgg tggagaagat tgtctaccac 1080
agcaagtaca agccaaagag gctgggcaat gacatcgccc ttatgaagct ggccgggcca 1140
ctcacgttca atggtacatc tgggtctcta tgtggttctg cagctcttcc tttgtttcaa 1200
gaggatttgc aattgctcat tgaagcattc ttatgatggc tgctttataa tccttgtcag 1260
atattaataa ttccaactcc tgattcatgt tggtgttggc atcagttgat tatcttttct 1320
cattaaaatt gtgatgctcc taaaaaaaaa aaaaaaaaa 1359

<210> 115
<211> 344
<212> PRT
<213> Homo sapiens

<400> 115
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Met Gly Glu Asn Asp Pro Pro Ala Val Glu Ala Pro Phe Ser Phe Arg
 1               5                  10                  15
Ser Leu Phe Gly Leu Asp Asp Leu Lys Ile Ser Pro Val Ala Pro Asp
            20                  25                  30
Ala Asp Ala Val Ala Ala Gln Ile Leu Ser Leu Leu Pro Leu Lys Phe
        35                  40                  45
Phe Pro Ile Ile Val Ile Gly Ile Ile Ala Leu Ile Leu Ala Leu Ala
    50                  55                  60
```

```
Ile Gly Leu Gly Ile His Phe Asp Cys Ser Gly Lys Tyr Arg Cys Arg
65                  70                  75                  80
Ser Ser Phe Lys Cys Ile Glu Leu Ile Ala Arg Cys Asp Gly Val Ser
                85                  90                  95
Asp Cys Lys Asp Gly Glu Asp Glu Tyr Arg Cys Val Arg Val Gly Gly
            100                 105                 110
Gln Asn Ala Val Leu Gln Val Phe Thr Ala Ala Ser Trp Lys Thr Met
        115                 120                 125
Cys Ser Asp Asp Trp Lys Gly His Tyr Ala Asn Val Ala Cys Ala Gln
    130                 135                 140
Leu Gly Phe Pro Ser Tyr Val Ser Ser Asp Asn Leu Arg Val Ser Ser
145                 150                 155                 160
Leu Glu Gly Gln Phe Arg Glu Glu Phe Val Ser Ile Asp His Leu Leu
                165                 170                 175
Pro Asp Asp Lys Val Thr Ala Leu His His Ser Val Tyr Val Arg Glu
            180                 185                 190
Gly Cys Ala Ser Gly His Val Val Thr Leu Gln Cys Thr Ala Cys Gly
        195                 200                 205
His Arg Arg Gly Tyr Ser Ser Arg Ile Val Gly Gly Asn Met Ser Leu
    210                 215                 220
Leu Ser Gln Trp Pro Trp Gln Ala Ser Leu Gln Phe Gln Gly Tyr His
225                 230                 235                 240
Leu Cys Gly Gly Ser Val Ile Thr Pro Leu Trp Ile Ile Thr Ala Ala
                245                 250                 255
His Cys Val Tyr Asp Leu Tyr Leu Pro Lys Ser Trp Thr Ile Gln Val
            260                 265                 270
Gly Leu Val Ser Leu Leu Asp Asn Pro Ala Pro Ser His Leu Val Glu
        275                 280                 285
Lys Ile Val Tyr His Ser Lys Tyr Lys Pro Lys Arg Leu Gly Asn Asp
    290                 295                 300
Ile Ala Leu Met Lys Leu Ala Gly Pro Leu Thr Phe Asn Gly Thr Ser
305                 310                 315                 320
Gly Ser Leu Cys Gly Ser Ala Ala Leu Pro Leu Phe Gln Glu Asp Leu
                325                 330                 335
Gln Leu Leu Ile Glu Ala Phe Leu
            340
```

<210> 116
<211> 1191
<212> DNA
<213> Homo sapiens

<400> 116
actgcagccg aaccctggtc cctcctccac aatgtggctt ctcctcactc tctccttcct 60
gctggcatcc acagcagccc aggatggtga caagttgctg gaaggtgacg agtgtgcacc 120
ccactcccag ccatggcaag tggctctcta cgagcgtgga cgctttaact gtggcgcttc 180
cctcatctcc ccacactggg tgctgtctgc ggcccactgc caaagccgct tcatgagagt 240
gcgcctggga gagcacaacc tgcgcaagcg cgatggccca gagcaactac ggaccacgtc 300
tcgggtcatt ccacacccgc gctacgaagc gcgcagccac cgcaacgaca tcatgttgct 360
gcgcctagtc cagcccgcac gcctgaaccc ccagtgagtc tcccagatac gttgcattgt 420
gccaacatca gcattatctc ggacacatct tgtgacaaga gctacccagg gcgcctgaca 480
aacaccatgg tgtgtgcagg cgcggagggc agaggcgcag aatcctgtga gggtgactct 540
gggggacccc tggtctgtgg gggcatcctg cagggcattg tgtcctgggg tgacgtccct 600
tgtgacaaca ccaccaagcc tggtgtctat accaaagtct gccactactt ggagtggatc 660
agggaaacca tgaagaggaa ctgactattc tagcctatct cctgtgcccc tgactgagca 720
gaagccccca cagctggcca gcagccccgc ctgacatgga acagaacgga gccatccccc 780
aagaccctgt ccaaggccca gatgttagcc aaggacttgt cccacctgag gacaaagctg 840

```
gcgctcaagg tcacctgttt aatgccaaga taacaaagcg ctgatccaag ttgctctgta 900
ggaatttctg tgacttttt ctggggtcaa agagaaaccc cgagacactg tacactgttc 960
cttttcaccc accaccccga tccctaggtg aggagaagcg gcttgaagca gggctccatt 1020
cattcaacac acatgaccac ccgtgtgatc ttgaacaaga ggcccaatct cacttcgcct 1080
tggtttcctt atctgtaaaa tgagaccatc ttattgctga cttcaaaggg ctgttgtgag 1140
gattaaatga gatgattcgt ctgaactgat taaaatcgtg tctggcactg a          1191
```

<210> 117
<211> 121
<212> PRT
<213> Homo sapiens

<400> 117

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Met Trp Leu Leu Leu Thr Leu Ser Phe Leu Leu Ala Ser Thr Ala Ala
 1               5                  10                  15
Gln Asp Gly Asp Lys Leu Leu Glu Gly Asp Glu Cys Ala Pro His Ser
            20                  25                  30
Gln Pro Trp Gln Val Ala Leu Tyr Glu Arg Gly Arg Phe Asn Cys Gly
        35                  40                  45
Ala Ser Leu Ile Ser Pro His Trp Val Leu Ser Ala Ala His Cys Gln
    50                  55                  60
Ser Arg Phe Met Arg Val Arg Leu Gly Glu His Asn Leu Arg Lys Arg
65                  70                  75                  80
Asp Gly Pro Glu Gln Leu Arg Thr Thr Ser Arg Val Ile Pro His Pro
                85                  90                  95
Arg Tyr Glu Ala Arg Ser His Arg Asn Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Val Gln Pro Ala Arg Leu Asn Pro Gln
        115                 120
```

<210> 118
<211> 1172
<212> DNA
<213> Homo sapiens

<400> 118

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actgcagccg aaccctggtc cctcctccac aatgtggctt ctcctcactc tctccttcct 60
gctggcatcc acagcagccc aggatggtga caagttgctg gaaggtgacg agtgtgcacc 120
ccactcccag ccatggcaag tggctctcta cgagcgtgga cgctttaact gtggcgcttc 180
cctcatctcc ccacactggg tgctgtctgc ggcccactgc caaagccgct tcatgagagt 240
gcgcctggga gagcacaacc tgcgcaagcg cgatggccca gagcaactac ggaccacgtc 300
tcgggtcatt ccacacccgc gctacgaagc gcgcagccac cgcaacgaca tcatgttgct 360
gcgcctagtc cagcccgcac gcctgaaccc ccaggtgcgc cccgcggtgc tacccacgcg 420
ttgcccccac ccgggggagg cctgtgtggt gtctggctgg ggcctggtgt cccacaacga 480
gcctgggacc gctgggagcc cccggtcaca agggtgactc tgggggaccc ctggtctgtg 540
ggggcatcct gcagggcatt gtgtcctggg gtgacgtccc ttgtgacaac accaccaagc 600
ctggtgtcta taccaaagtc tgccactact tggagtggat cagggaaacc atgaagagga 660
actgactatt ctagcctatc tcctgtgccc ctgactgagc agaagccccc acagctggcc 720
agcagccccg cctgacatgg aacagaacgg agccatcccc caagaccctg tccaaggccc 780
agatgttagc caaggacttg tcccacctga ggacaaagct ggcgctcaag gtcacctgtt 840
taatgccaag ataacaaagc gctgatccaa gttgctctgt aggaatttct gtgacttttt 900
tctggggtca aagagaaacc ccgagacact gtacactgtt ccttttcacc caccaccccg 960
atccctaggt gaggagaagc ggcttgaagc agggctccat tcattcaaca cacatgacca 1020
cccgtgtgat cttgaacaag aggcccaatc tcacttcgcc ttggtttcct tatctgtaaa 1080
atgagaccat cttattgctg acttcaaagg gctgttgtga ggattaaatg agatgattcg 1140
tctgaactga ttaaaatcgt gtctggcact ga                              1172
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<210> 119
<211> 161
<212> PRT
<213> Homo sapiens

<400> 119
Met Trp Leu Leu Leu Thr Leu Ser Phe Leu Leu Ala Ser Thr Ala Ala
1 5 10 15
Gln Asp Gly Asp Lys Leu Leu Glu Gly Asp Glu Cys Ala Pro His Ser
20 25 30
Gln Pro Trp Gln Val Ala Leu Tyr Glu Arg Gly Arg Phe Asn Cys Gly
35 40 45
Ala Ser Leu Ile Ser Pro His Trp Val Leu Ser Ala Ala His Cys Gln
50 55 60
Ser Arg Phe Met Arg Val Arg Leu Gly Glu His Asn Leu Arg Lys Arg
65 70 75 80
Asp Gly Pro Glu Gln Leu Arg Thr Thr Ser Arg Val Ile Pro His Pro
85 90 95
Arg Tyr Glu Ala Arg Ser His Arg Asn Asp Ile Met Leu Leu Arg Leu
100 105 110
Val Gln Pro Ala Arg Leu Asn Pro Gln Val Arg Pro Ala Val Leu Pro
115 120 125
Thr Arg Cys Pro His Pro Gly Glu Ala Cys Val Val Ser Gly Trp Gly
130 135 140
Leu Val Ser His Asn Glu Pro Gly Thr Ala Gly Ser Pro Arg Ser Gln
145 150 155 160
Gly

<210> 120
<211> 1054
<212> DNA
<213> Homo sapiens

<400> 120
actgcagccg aaccctggtc cctcctccac aatgtggctt ctcctcactc tctccttcct 60
gctggcatcc acagcagccc aggatggtga caagttgctg gaaggtgacg agtgtgcacc 120
ccactcccag ccatggcaag tggctctcta cgagcgtgga cgctttaact gtggcgcttc 180
cctcatctcc ccacactggg tgctgtctgc ggcccactgc caaagccgct tcatgagagt 240
gcgcctggga gagcacaacc tgcgcaagcg cgatggccca gagcaactac ggaccacgtc 300
tcgggtcatt ccacacccgc gctacgaagc gcgcagccac cgcaacgaca tcatgttgct 360
gcgcctagtc cagcccgcac gcctgaaccc ccagggtgac tctgggggac ccctggtctg 420
tgggggcatc ctgcagggca ttgtgtcctg gggtgacgtc ccttgtgaca acaccaccaa 480
gcctggtgtc tataccaaag tctgccacta cttggagtgg atcagggaaa ccatgaagag 540
gaactgacta ttctagccta tctcctgtgc ccctgactga gcagaagccc ccacagctgg 600
ccagcagccc cgcctgacat ggaacagaac ggagccatcc cccaagaccc tgtccaaggc 660
ccagatgtta gccaaggact tgtcccacct gaggacaaag ctggcgctca aggtcacctg 720
tttaatgcca agataacaaa gcgctgatcc aagttgctct gtaggaattt ctgtgacttt 780
tttctggggt caaagagaaa ccccgagaca ctgtacactg ttccttttca cccaccaccc 840
cgatccctag gtgaggagaa gcggcttgaa gcagggctcc attcattcaa cacacatgac 900
cacccgtgtg atcttgaaca agaggcccaa tctcacttcg ccttggtttc cttatctgta 960
aaatgagacc atcttattgc tgacttcaaa gggctgttgt gaggattaaa tgagatgatt 1020
cgtctgaact gattaaaatc gtgtctggca ctga 1054

<210> 121
<211> 171
<212> PRT

<213> Homo sapiens

<400> 121

```
Met Trp Leu Leu Leu Thr Leu Ser Phe Leu Leu Ala Ser Thr Ala Ala
 1               5                  10                  15
Gln Asp Gly Asp Lys Leu Leu Glu Gly Asp Glu Cys Ala Pro His Ser
            20                  25                  30
Gln Pro Trp Gln Val Ala Leu Tyr Glu Arg Gly Arg Phe Asn Cys Gly
        35                  40                  45
Ala Ser Leu Ile Ser Pro His Trp Val Leu Ser Ala Ala His Cys Gln
    50                  55                  60
Ser Arg Phe Met Arg Val Arg Leu Gly Glu His Asn Leu Arg Lys Arg
65                  70                  75                  80
Asp Gly Pro Glu Gln Leu Arg Thr Thr Ser Arg Val Ile Pro His Pro
                85                  90                  95
Arg Tyr Glu Ala Arg Ser His Arg Asn Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Val Gln Pro Ala Arg Leu Asn Pro Gln Gly Asp Ser Gly Gly Pro Leu
        115                 120                 125
Val Cys Gly Gly Ile Leu Gln Gly Ile Val Ser Trp Gly Asp Val Pro
    130                 135                 140
Cys Asp Asn Thr Thr Lys Pro Gly Val Tyr Thr Lys Val Cys His Tyr
145                 150                 155                 160
Leu Glu Trp Ile Arg Glu Thr Met Lys Arg Asn
                165                 170
```

<210> 122
<211> 1309
<212> DNA
<213> Homo sapiens

<400> 122

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actgcagccg aaccctggtc cctcctccac aatgtggctt ctcctcactc tctccttcct 60
gctggcatcc acagcagccc aggatggtga caagttgctg gaaggtgacg agtgtgcacc 120
ccactcccag ccatggcaag tggctctcta cgagcgtgga cgctttaact gtggcgcttc 180
cctcatctcc ccacactggg tgctgtctgc ggcccactgc caaagccgct tcatgagagt 240
gcgcctggga gagcacaacc tgcgcaagcg cgatggccca gagcaactac ggaccacgtc 300
tcgggtcatt ccacacccgc gctacgaagc gcgcagccac cgcaacgaca tcatgttgct 360
gcgcctagtc cagcccgcac gcctgaaccc ccaggtgcgc cccgcggtgc tacccacgcg 420
ttgcccccac ccgggggagg cctgtgtggt gtctggctgg ggcctggtgt cccacaacga 480
gcctgggacc gctgggagcc cccggtcaca agtgagtctc ccagatacgt tgcattgtgc 540
caacatcagc attatctcgg acacatcttg tgacaagagc tacccagggc gcctgacaaa 600
caccatggtg tgtgcaggcg cggagggcag aggcgcagaa tcctgtgagg gtgactctgg 660
gggacccctg gtctgtgggg gcatcctgca gggcattgtg tcctggggtg acgtcccttg 720
tgacaacacc accaagcctg gtgtctatac caaagtctgc cactacttgg agtggatcag 780
ggaaaccatg aagaggaact gactattcta gcctatctcc tgtgcccctg actgagcaga 840
agcccccaca gctggccagc agccccgcct gacatggaac agaacggagc catccccaa 900
gaccctgtcc aaggcccaga tgttagccaa ggacttgtcc cacctgagga caaagctggc 960
gctcaaggtc acctgtttaa tgccaagata acaaagcgct gatccaagtt gctctgtagg 1020
aatttctgtg actttttttct ggggtcaaag agaaaccccg agacactgta cactgttcct 1080
tttcacccac caccccgatc cctaggtgag gagaagcggc ttgaagcagg gctccattca 1140
ttcaacacac atgaccaccc gtgtgatctt gaacaagagg cccaatctca cttcgccttg 1200
gtttccttat ctgtaaaatg agaccatctt attgctgact tcaaagggct gttgtgagga 1260
ttaaatgaga tgattcgtct gaactgatta aaatcgtgtc tggcactga              1309
```

<210> 123
<211> 256

<212> PRT
<213> Homo sapiens

<400> 123

```
Met Trp Leu Leu Leu Thr Leu Ser Phe Leu Leu Ala Ser Thr Ala Ala
 1               5                  10                  15
Gln Asp Gly Asp Lys Leu Leu Glu Gly Asp Glu Cys Ala Pro His Ser
            20                  25                  30
Gln Pro Trp Gln Val Ala Leu Tyr Glu Arg Gly Arg Phe Asn Cys Gly
        35                  40                  45
Ala Ser Leu Ile Ser Pro His Trp Val Leu Ser Ala Ala His Cys Gln
    50                  55                  60
Ser Arg Phe Met Arg Val Arg Leu Gly Glu His Asn Leu Arg Lys Arg
65                  70                  75                  80
Asp Gly Pro Glu Gln Leu Arg Thr Thr Ser Arg Val Ile Pro His Pro
                85                  90                  95
Arg Tyr Glu Ala Arg Ser His Arg Asn Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Val Gln Pro Ala Arg Leu Asn Pro Gln Val Arg Pro Ala Val Leu Pro
        115                 120                 125
Thr Arg Cys Pro His Pro Gly Glu Ala Cys Val Val Ser Gly Trp Gly
    130                 135                 140
Leu Val Ser His Asn Glu Pro Gly Thr Ala Gly Ser Pro Arg Ser Gln
145                 150                 155                 160
Val Ser Leu Pro Asp Thr Leu His Cys Ala Asn Ile Ser Ile Ile Ser
                165                 170                 175
Asp Thr Ser Cys Asp Lys Ser Tyr Pro Gly Arg Leu Thr Asn Thr Met
            180                 185                 190
Val Cys Ala Gly Ala Glu Gly Arg Gly Ala Glu Ser Cys Glu Gly Asp
        195                 200                 205
Ser Gly Gly Pro Leu Val Cys Gly Gly Ile Leu Gln Gly Ile Val Ser
    210                 215                 220
Trp Gly Asp Val Pro Cys Asp Asn Thr Thr Lys Pro Gly Val Tyr Thr
225                 230                 235                 240
Lys Val Cys His Tyr Leu Glu Trp Ile Arg Glu Thr Met Lys Arg Asn
                245                 250                 255
```

<210> 124
<211> 920
<212> DNA
<213> Homo sapiens

<400> 124

```
cagacaggag gcgtctgtag agatatcatg aacttcaact tagctttgtt ttccagagac 60
tggagctaaa ctgggctttc aacatcatca tgaagtttat cctcctctgg gccctcttga 120
atctgactgt tgctttggcc tttaatccag attacacagt cagctccact ccccttact 180
tggtctattt gaaatctgac tacttgccct gcgctggagt cctgatccac ccgctttggg 240
tgatcacagc tgcacactgc aatttaccaa agcttcgggt gatattgggg gttacaatcc 300
cagcagactc taatgaaaag catctgcaag tgattggcta tgagaagatg attcatcatc 360
cacacttctc agtcacttct attgatcatg acatcatgct aatcaagctg aaaacagagg 420
ctgaactcaa tgactatgtg aaattagcca acctgcccta ccaaactatc tctgaaaata 480
ccatgtgctc tgtctctacc tggagctaca atgtgtgtga tatctacaaa gagcccgatt 540
cactgcaaac tgtgaacatc tctgtaatct ccaagcctca gtgtcgcgat gcctataaaa 600
cctacaacat cacggaaaat atgctgtgtg tgggcattgt gccaggaagg aggcagccct 660
gcaaggaagt ttctgctgcc ccggcaatct gcaatgggat gcttcaagga atcctgtctt 720
ttgcggatgg atgtgttttg agagccgatg ttggcatcta tgccaaaatt ttttactata 780
taccctggat tgaaaatgta atccaaaata actgagctgt ggcagttgtg gaccatatga 840
```

cacagcttgt ccccatcgtt cacctttaga attaaatata aattaactcc tcaaaaaaaa 900
aaaaaaaaaa aaaaaaaaaa 920

<210> 125
<211> 241
<212> PRT
<213> Homo sapiens

<400> 125
Met Lys Phe Ile Leu Leu Trp Ala Leu Leu Asn Leu Thr Val Ala Leu
1 5 10 15
Ala Phe Asn Pro Asp Tyr Thr Val Ser Ser Thr Pro Pro Tyr Leu Val
20 25 30
Tyr Leu Lys Ser Asp Tyr Leu Pro Cys Ala Gly Val Leu Ile His Pro
35 40 45
Leu Trp Val Ile Thr Ala Ala His Cys Asn Leu Pro Lys Leu Arg Val
50 55 60
Ile Leu Gly Val Thr Ile Pro Ala Asp Ser Asn Glu Lys His Leu Gln
65 70 75 80
Val Ile Gly Tyr Glu Lys Met Ile His His Pro His Phe Ser Val Thr
85 90 95
Ser Ile Asp His Asp Ile Met Leu Ile Lys Leu Lys Thr Glu Ala Glu
100 105 110
Leu Asn Asp Tyr Val Lys Leu Ala Asn Leu Pro Tyr Gln Thr Ile Ser
115 120 125
Glu Asn Thr Met Cys Ser Val Ser Thr Trp Ser Tyr Asn Val Cys Asp
130 135 140
Ile Tyr Lys Glu Pro Asp Ser Leu Gln Thr Val Asn Ile Ser Val Ile
145 150 155 160
Ser Lys Pro Gln Cys Arg Asp Ala Tyr Lys Thr Tyr Asn Ile Thr Glu
165 170 175
Asn Met Leu Cys Val Gly Ile Val Pro Gly Arg Arg Gln Pro Cys Lys
180 185 190
Glu Val Ser Ala Ala Pro Ala Ile Cys Asn Gly Met Leu Gln Gly Ile
195 200 205
Leu Ser Phe Ala Asp Gly Cys Val Leu Arg Ala Asp Val Gly Ile Tyr
210 215 220
Ala Lys Ile Phe Tyr Tyr Ile Pro Trp Ile Glu Asn Val Ile Gln Asn
225 230 235 240
Asn

<210> 126
<211> 2393
<212> DNA
<213> Homo sapiens

<400> 126
cgcccgggca ggttgagaag ccaggggcca agatggatct tctcctcgac atcagctaag 60
cctggaggac tcttcccctc agagaccatg gagagggaca gccacgggaa tgcatctcca 120
gcaagaacac cttcagctgg agcatctcca gcccaggcat ctccagctgg gacacctcca 180
ggccgggcat ctccagccca ggcatctcca gcccaggcat ctccagctgg gacacctccg 240
ggccgggcat ctccagccca ggcatctcca gctggtacac ctccaggccg ggcatctcca 300
ggccgggcat ctccagccca ggcatctcca gcccgggcat ctccggctct ggcatcactt 360
tccaggtcct catccggcag gtcatcatcc gccaggtcag cctcggtgac aacctcccca 420
accagagtgt accttgttag agcaacacca gtgggggctg tacccatccg atcatctcct 480
gccaggtcag caccagcaac cagggccacc agggagagcc caggtacgag cctgcccaag 540

```
ttcacctggc gggagggcca gaagcagcta ccgctcatcg ggtgcgtgct cctcctcatt 600
gccctggtgg tttcgctcat catcctcttc cagttctggc agggccacac agggatcagg 660
cacaaggagc agagggagag ctgtcccaag cacgctgttc gctgtgacgg ggtggtggac 720
tgcaagctga agagtgacga gctgggctgc gtgaggtttg actgggacaa gtctctgctt 780
aaaatctact ctgggtcctc ccatcagtgg cttcccatct gtagcagcaa ctggaatgac 840
tcctactcag agaagacctg ccagcagctg ggtttcgaga gtgctcaccg gacaaccgag 900
gttgcccaca gggattttgc caacagcttc tcaatcttga gatacaactc caccatccag 960
gaaagcctcc acaggtctga atgcccttcc cagcggtata tctccctcca gtgttcccac 1020
tgcggactga gggccatgac cgggcggatc gtgggagggg cgctggcctc ggatagcaag 1080
tggccttggc aagtgagtct gcacttcggc accacccaca tctgtggagg cacgctcatt 1140
gacgcccagt gggtgctcac tgccgcccac tgcttcttcg tgacccggga gaaggtcctg 1200
gagggctgga aggtgtacgc gggcaccagc aacctgcacc agttgcctga ggcagcctcc 1260
attgccgaga tcatcatcaa cagcaattac accgatgagg aggacgacta tgacatcgcc 1320
ctcatgcggc tgtccaagcc cctgaccctg tccgctcaca tccaccctgc ttgcctcccc 1380
atgcatggac agacctttag cctcaatgag acctgctgga tcacaggctt tggcaagacc 1440
agggagacag atgacaagac atcccccttc ctccgggagg tgcaggtcaa tctcatcgac 1500
ttcaagaaat gcaatgacta cttggtctat gacagttacc ttaccccaag gatgatgtgt 1560
gctggggacc ttcgtggggg cagagactcc tgccagggag acagcggggg gcctcttgtc 1620
tgtgagcaga acaaccgctg gtacctggca ggtgtcacca gctggggcac aggctgtggc 1680
cagagaaaca aacctggtgt gtacaccaaa gtgacagaag ttcttccctg gatttacagc 1740
aagatggagg taagatccct gcagcaggac actgcaccca gcaggctggg aacttcctca 1800
ggtggggacc ctggaggagc acccagggtg taggcagagg tcccctcagc gtccccatat 1860
tcgggggggtg ttctggacag ggtcaaatgt gatgcctggg gtcaatccca gctgtctgtg 1920
tttctttccc tgcttttctt ccctcagaac agagctcagc gggttgaaaa agggtggacc 1980
tacaggccag gcaggcagtt gctgggcaga tgttctccca gaagtatttt tttgtgtaag 2040
gttgcaatgg actttgaaaa cgtttcagtt tctgcagagg attttgtgat agtctttgtt 2100
atcaagcatt tatgcatggg aatccgctct tcatggcctt tcccagctct gtttgtttta 2160
gtctttttga ttttctttt gttgttgttg ttgtcttttt ttaaaaacac aagtgactcc 2220
attttaactc tgacaacttt cacagctgtc accagaatgc tccctgagaa ctaccattct 2280
ttcccttcc cacttaaaat atttcatcag aacctcacca ctatcataaa agagtataaa 2340
gtaataaaat aataaaaagc gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa        2393
```

<210> 127
<211> 581
<212> PRT
<213> Homo Sapiens

<400> 127

```
Met Glu Arg Asp Ser His Gly Asn Ala Ser Pro Ala Arg Thr Pro Ser
 1               5                  10                  15
Ala Gly Ala Ser Pro Ala Gln Ala Ser Pro Ala Gly Thr Pro Pro Gly
            20                  25                  30
Arg Ala Ser Pro Ala Gln Ala Ser Pro Ala Gln Ala Ser Pro Ala Gly
        35                  40                  45
Thr Pro Pro Gly Arg Ala Ser Pro Ala Gln Ala Ser Pro Ala Gly Thr
    50                  55                  60
Pro Pro Gly Arg Ala Ser Pro Gly Arg Ala Ser Pro Ala Gln Ala Ser
65                  70                  75                  80
Pro Ala Arg Ala Ser Pro Ala Leu Ala Ser Leu Ser Arg Ser Ser Ser
                85                  90                  95
Gly Arg Ser Ser Ser Ala Arg Ser Ala Ser Val Thr Thr Ser Pro Thr
            100                 105                 110
Arg Val Tyr Leu Val Arg Ala Thr Pro Val Gly Ala Val Pro Ile Arg
        115                 120                 125
Ser Ser Pro Ala Arg Ser Ala Pro Ala Thr Arg Ala Thr Arg Glu Ser
    130                 135                 140
Pro Gly Thr Ser Leu Pro Lys Phe Thr Trp Arg Glu Gly Gln Lys Gln
145                 150                 155                 160
```

```
Leu Pro Leu Ile Gly Cys Val Leu Leu Leu Ile Ala Leu Val Val Ser
                165                 170                 175
Leu Ile Ile Leu Phe Gln Phe Trp Gln Gly His Thr Gly Ile Arg His
            180                 185                 190
Lys Glu Gln Arg Glu Ser Cys Pro Lys His Ala Val Arg Cys Asp Gly
        195                 200                 205
Val Val Asp Cys Lys Leu Lys Ser Asp Glu Leu Gly Cys Val Arg Phe
    210                 215                 220
Asp Trp Asp Lys Ser Leu Leu Lys Ile Tyr Ser Gly Ser Ser His Gln
225                 230                 235                 240
Trp Leu Pro Ile Cys Ser Ser Asn Trp Asn Asp Ser Tyr Ser Glu Lys
                245                 250                 255
Thr Cys Arg Gln Leu Gly Phe Glu Ser Ala His Arg Thr Thr Glu Val
            260                 265                 270
Ala His Arg Asp Phe Ala Asn Ser Phe Ser Ile Leu Arg Tyr Asn Ser
        275                 280                 285
Thr Ile Gln Glu Ser Leu His Arg Ser His Cys Pro Ser Gln Arg Tyr
    290                 295                 300
Ile Ser Leu Gln Cys Ser His Cys Gly Leu Arg Ala Met Thr Gly Arg
305                 310                 315                 320
Ile Val Gly Gly Ala Leu Ala Ser Asp Ser Lys Trp Pro Trp Gln Val
                325                 330                 335
Ser Leu His Phe Gly Thr Thr His Ile Cys Gly Gly Thr Leu Ile Asp
            340                 345                 350
Ala Gln Trp Val Leu Thr Ala Ala His Cys Phe Phe Val Thr Arg Glu
        355                 360                 365
Lys Val Leu Glu Gly Trp Lys Val Tyr Ala Gly Thr Ser Asn Leu His
    370                 375                 380
Gln Leu Pro Glu Ala Ala Ser Ile Ala Glu Ile Ile Ile Asn Ser Asn
385                 390                 395                 400
Tyr Thr Asp Glu Glu Asp Asp Tyr Asp Ile Ala Leu Met Arg Leu Ser
                405                 410                 415
Lys Pro Leu Thr Leu Ser Ala His Ile His Pro Ala Cys Leu Pro Met
            420                 425                 430
His Gly Gln Thr Phe Ser Leu Asn Glu Thr Cys Trp Ile Thr Gly Phe
        435                 440                 445
Gly Lys Thr Arg Glu Thr Asp Asp Lys Thr Ser Pro Phe Leu Arg Glu
    450                 455                 460
Val Gln Val Asn Leu Ile Asp Phe Lys Lys Cys Asn Asp Tyr Leu Val
465                 470                 475                 480
Tyr Asp Ser Tyr Leu Thr Pro Arg Met Met Cys Ala Gly Asp Leu His
                485                 490                 495
Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
            500                 505                 510
Glu Gln Asn Asn Arg Trp Tyr Leu Ala Gly Val Thr Ser Trp Gly Thr
        515                 520                 525
Gly Cys Gly Gln Arg Asn Lys Pro Gly Val Tyr Thr Lys Val Thr Glu
    530                 535                 540
Val Leu Pro Trp Ile Tyr Ser Lys Met Glu Val Arg Ser Leu Gln Gln
545                 550                 555                 560
Asp Thr Ala Pro Ser Arg Leu Gly Thr Ser Ser Gly Gly Asp Pro Gly
                565                 570                 575
Gly Ala Pro Arg Val
            580
```

<210> 128
<211> 148

<212> PRT
<213> Homo sapiens

<400> 128
Cys Gly Lys Pro Lys Val Val Gly Lys Ile Tyr Gly Gly Arg Asp Ala
 1   5   10   15
Ala Ala Gly Gln Trp Pro Trp Gln Ala Ser Leu Leu Tyr Trp Gly Ser
            20   25   30
His Leu Cys Gly Ala Val Leu Ile Asp Ser Cys Trp Leu Val Ser Thr
        35   40   45
Thr His Cys Phe Leu Asn Lys Ser Gln Ala Pro Lys Asn Tyr Gln Val
    50   55   60
Leu Leu Gly Asn Ile Gln Leu Tyr His Gln Thr Gln His Thr Gln Lys
65   70   75   80
Met Ser Val His Arg Ile Ile Thr His Pro Asp Phe Glu Lys Leu His
                85   90   95
Pro Phe Gly Ser Asp Ile Ala Met Leu Gln Leu His Leu Pro Met Asn
            100   105   110
Phe Thr Ser Tyr Ile Val Pro Val Cys Leu Pro Ser Arg Asp Met Gln
        115   120   125
Leu Pro Ser Asn Val Ser Cys Trp Ile Thr Gly Trp Gly Met Ala Ile
    130   135   140
Leu Gly Gly Leu
145

<210> 129
<211> 712
<212> DNA
<213> Homo sapiens

<400> 129
cacagagggc tccagcgtga ttgccactgg ttaatgacct gccacccccg ccccccccaac 60
ctctggtgcc gtccaaggac tctgacccca gtgcagtgtc tgtagggaag aggagccatg 120
gggcttcggg caggccccat cctgcttctg ctgctgtggc tgctgccaga atgcggccac 180
tccaaggagg ccgggaggat tgtgggaggc caagacaccc aggaaggacg ctggccgtgg 240
caggttggcc tgtggttgac ctcagtgggg catgtatgtg ggggcttcct catccaccca 300
cgctgggtgc tcacagccgc ccactgcttc ctgagggtga ctccgggggg ccgctggtct 360
gccccatcaa tgatacgtgg atccaggccg gcattgtgag ctggggattc ggctgtgccc 420
ggcctttccg gcctggtgtc tacacccagg tgctaagcta cacagactgg attcagagaa 480
ccctggctga atctcactca ggcatgtctg gggcccgccc aggtgcccca ggatcccact 540
caggcacctc cagatcccac ccagtgctgc tgcttgagct gttgaccgta tgcttgcttg 600
ggtccctgtg aaccatgagc catggagtcc gggatcccct ttctggtagg attgatggaa 660
tctaataata aaaactgtag gttttttatg tgaaaaaaaa aaaaaaaaaa aa   712

<210> 130
<211> 146
<212> PRT
<213> Homo sapiens

<400> 130
Met Arg Pro Leu Gln Gly Gly Arg Glu Asp Cys Gly Arg Pro Arg His
 1   5   10   15
Pro Gly Arg Thr Leu Ala Val Ala Gly Trp Pro Val Val Asp Leu Ser
            20   25   30
Gly Ala Cys Met Trp Gly Leu Pro His Pro Pro Thr Leu Gly Ala His
        35   40   45
Ser Arg Pro Leu Leu Pro Glu Gly Asp Ser Gly Gly Pro Leu Val Cys

```
     50                  55                  60
Pro Ile Asn Asp Thr Trp Ile Gln Ala Gly Ile Val Ser Trp Gly Phe
65                  70                  75                  80
Gly Cys Ala Arg Pro Phe Arg Pro Gly Val Tyr Thr Gln Val Leu Ser
                85                  90                  95
Tyr Thr Asp Trp Ile Gln Arg Thr Leu Ala Glu Ser His Ser Gly Met
            100                 105                 110
Ser Gly Ala Arg Pro Gly Ala Pro Gly Ser His Ser Gly Thr Ser Arg
        115                 120                 125
Ser His Pro Val Leu Leu Leu Glu Leu Leu Thr Val Cys Leu Leu Gly
    130                 135                 140
Ser Leu
145
```

<210> 131
<211> 800
<212> DNA
<213> Homo sapiens

<400> 131
```
accaccatga atccactcct gatccttacc tttgtggcag ctgctcttgc tgccccctttt 60
gatgatgatg acaagatcgt tgggggctac aactgtgagg agaattctgt cccctaccag 120
gtgtccctga attctggcta ccacttctgt ggtggctccc tcatcaacga acagtgggtg 180
gtatcagcag gccactgcta caagtcccgc atccaggtga gactgggaga gcacaacatc 240
gaagtcctgg aggggaatga gcagttcatc aatgcagcca agatcatccg ccacccccaa 300
tacgacagga agactctgaa caatgacatc atgttaatca agctctcctc acgtgcagta 360
atcaacgccc gcgtgtccac catctctctg cccaccgccc ctccagccac tggcacgaag 420
tgcctcatct ctggctgggg caacactgcg agctctggcg ccgactaccc agacgagctg 480
cagtgcctgg acgctcctgt gctgagccag gctaagtgtg aagcctccta ccctggaaag 540
attaccagca acatgttctg tgtgggcttc cttgagggag gcaaggattc atgtcagggt 600
gattctggtg gccctgtggt ctgcaatgga cagctccaag gagttgtctc ctggggtgat 660
ggctgtgccc agaagaacaa gcctggagtc tacaccaagg tctacaacta tgtgaaatgg 720
attaagaaca ccatagctgc caatagctaa agcccccagt atctcttcag tctctatacc 780
aataaagtga ccctgttctc                                             800
```

<210> 132
<211> 247
<212> PRT
<213> Homo sapiens

<400> 132
```
Met Asn Pro Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Leu Ala Ala
 1               5                  10                  15
Pro Phe Asp Asp Asp Asp Lys Ile Val Gly Gly Tyr Asn Cys Glu Glu
            20                  25                  30
Asn Ser Val Pro Tyr Gln Val Ser Leu Asn Ser Gly Tyr His Phe Cys
        35                  40                  45
Gly Gly Ser Leu Ile Asn Glu Gln Trp Val Val Ser Ala Gly His Cys
    50                  55                  60
Tyr Lys Ser Arg Ile Gln Val Arg Leu Gly Glu His Asn Ile Glu Val
65                  70                  75                  80
Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile Ile Arg His
                85                  90                  95
Pro Gln Tyr Asp Arg Lys Thr Leu Asn Asn Asp Ile Met Leu Ile Lys
            100                 105                 110
Leu Ser Ser Arg Ala Val Ile Asn Ala Arg Val Ser Thr Ile Ser Leu
        115                 120                 125
```

```
Pro Thr Ala Pro Pro Ala Thr Gly Thr Lys Cys Leu Ile Ser Gly Trp
    130                 135                 140
Gly Asn Thr Ala Ser Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys
145                 150                 155                 160
Leu Asp Ala Pro Val Leu Ser Gln Ala Lys Cys Glu Ala Ser Tyr Pro
                165                 170                 175
Gly Lys Ile Thr Ser Asn Met Phe Cys Val Gly Phe Leu Glu Gly Gly
            180                 185                 190
Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Val Val Cys Asn Gly
        195                 200                 205
Gln Leu Gln Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln Lys Asn
    210                 215                 220
Lys Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Lys Trp Ile Lys
225                 230                 235                 240
Asn Thr Ile Ala Ala Asn Ser
                245
```

<210> 133
<211> 938
<212> DNA
<213> Homo sapiens

<400> 133

```
gcacggaggg gcagagaccc cggagcccca gccccaccat gaccctcggc cgccgactcg 60
cgtgtctttt cctcgcctgt gtcctgccgg ccttgctgct gggggggcacc gcgctggcct 120
cggagattgt gggggggccgg cgagcgcggc cccacgcgtg gcccttcatg gtgtccctgc 180
agctgcgcgg aggccacttc tgcggcgcca ccctgattgc gcccaacttc gtcatgtcgg 240
ccgcgcactg cgtggcgaat gtaaacgtcc gcgcggtgcg ggtggtcctg ggagcccata 300
acctctcgcg gcgggagccc acccggcagg tgttcgccgt gcagcgcatc ttcgaaaacg 360
gctacgaccc cgtaaacttg ctcaacgaca tcgtgattct ccagctcaac gggtcggcca 420
ccatcaacgc caacgtgcag gtggcccagc tgccggctca gggacgccgc ctgggcaacg 480
gggtgcagtg cctggccatg ggctggggcc ttctgggcag gaaccgtggg atcgccagcg 540
tcctgcagga gctcaacgtg acggtggtga cgtccctctg ccgtcgcagc aacgtctgca 600
ctctcgtgag gggccggcag gccggcgtct gtttcgggga ctccggcagc cccttggtct 660
gcaacgggct aatccacgga attgcctcct tcgtccgggg aggctgcgcc tcagggctct 720
accccgatgc ctttgccccg gtggcacagt ttgtaaactg gatcgactct atcatccaac 780
gctccgagga caacccctgt ccccaccccc gggacccgga cccggccagc aggacccact 840
gagaagggct gcccgggtca cctcagctgc ccacacccac actctccagc atctggcaca 900
ataaacattc tctgttttgt agaaaaaaaa aaaaaaaa                        938
```

<210> 134
<211> 267
<212> PRT
<213> Homo sapiens

<400> 134

```
Met Thr Leu Gly Arg Arg Leu Ala Cys Leu Phe Leu Ala Cys Val Leu
 1               5                  10                  15
Pro Ala Leu Leu Leu Gly Gly Thr Ala Leu Ala Ser Glu Ile Val Gly
            20                  25                  30
Gly Arg Arg Ala Arg Pro His Ala Trp Pro Phe Met Val Ser Leu Gln
        35                  40                  45
Leu Arg Gly Gly His Phe Cys Gly Ala Thr Leu Ile Ala Pro Asn Phe
    50                  55                  60
Val Met Ser Ala Ala His Cys Val Ala Asn Val Asn Val Arg Ala Val
65                  70                  75                  80
Arg Val Val Leu Gly Ala His Asn Leu Ser Arg Arg Glu Pro Thr Arg
```

```
                85                  90                  95
Gln Val Phe Ala Val Gln Arg Ile Phe Glu Asn Gly Tyr Asp Pro Val
            100                 105                 110
Asn Leu Leu Asn Asp Ile Val Ile Leu Gln Leu Asn Gly Ser Ala Thr
        115                 120                 125
Ile Asn Ala Asn Val Gln Val Ala Gln Leu Pro Ala Gln Gly Arg Arg
    130                 135                 140
Leu Gly Asn Gly Val Gln Cys Leu Ala Met Gly Trp Gly Leu Leu Gly
145                 150                 155                 160
Arg Asn Arg Gly Ile Ala Ser Val Leu Gln Glu Leu Asn Val Thr Val
                165                 170                 175
Val Thr Ser Leu Cys Arg Arg Ser Asn Val Cys Thr Leu Val Arg Gly
            180                 185                 190
Arg Gln Ala Gly Val Cys Phe Gly Asp Ser Gly Ser Pro Leu Val Cys
        195                 200                 205
Asn Gly Leu Ile His Gly Ile Ala Ser Phe Val Arg Gly Gly Cys Ala
    210                 215                 220
Ser Gly Leu Tyr Pro Asp Ala Phe Ala Pro Val Ala Gln Phe Val Asn
225                 230                 235                 240
Trp Ile Asp Ser Ile Ile Gln Arg Ser Glu Asp Asn Pro Cys Pro His
                245                 250                 255
Pro Arg Asp Pro Asp Pro Ala Ser Arg Thr His
            260                 265
```

<210> 135
<211> 3895
<212> DNA
<213> Homo sapiens

<400> 135

```
attccggcac agggacacaa acaagctcac ccaacaaagc caagctggga ggaccaaggc 60
cgggcagccg ggagcaccca aggcaggaaa atgaggtggc tgcttctcta ttatgctctg 120
tgcttctccc tgtcaaaggc ttcagcccac accgtggagc taaacaatat gtttggccag 180
atccagtcgc ctggttatcc agactcctat cccagtgatt cagaggtgac ttggaatatc 240
actgtcccag atgggtttcg gatcaagctt tacttcatgc acttcaactt ggaatcctcc 300
tacctttgtg aatatgacta tgtgaaggta gaaactgagg accaggtgct ggcaaccttc 360
tgtggcaggg agaccacaga cacagagcag actcccggcc aggaggtggt cctctcccct 420
ggctccttca tgtccatcac tttccggtca gatttctcca atgaggagcg tttcacaggc 480
tttgatgccc actacatggc tgtggatgtg gacgagtgca aggagaggga ggacgaggag 540
ctgtcctgtg accactactg ccacaactac attggcggct actactgctc ctgccgcttc 600
ggctacatcc tccacacaga caacaggacc tgccgagtgg agtgcagtga caacctcttc 660
actcaaagga ctggggtgat caccagccct gacttcccaa acccttaccc caagagctct 720
gaatgcctgt ataccatcga gctggaggag ggtttcatgg tcaacctgca gtttgaggac 780
atatttgaca ttgaggacca tcctgaggtg ccctgccccc atgactacat caagatcaaa 840
gttggtccaa aagttttggg gcctttctgt ggagagaaag ccccagaacc catcagcacc 900
cagagccaca gtgtcctgat cctgttccat agtgacaact cgggagagaa ccggggctgg 960
aggctctcat acagggctgc aggaaatgag tgcccagagc tacagcctcc tgtccatggg 1020
aaaatcgagc cctcccaagc caagtatttc ttcaaagacc aagtgctcgt cagctgtgac 1080
acaggctaca aagtgctgaa ggataatgtg gagatggaca cattccagat tgagtgtctg 1140
aaggatggga cgtggagtaa caagattccc acctgtaaaa ttgtagactg tagagcccca 1200
ggagagctgg aacacgggct gatcaccttc tctacaagga acaacctcac cacatacaag 1260
tctgagatca aatactcctg tcaggagccc tattacaaga tgctcaacaa taacacaggt 1320
atatatacct gttctgccca aggagtctgg atgaataaag tattggggag aagcctaccc 1380
acctgccttc cagagtgtgg tcagccctcc cgctccctgc caagcctggt caagaggatc 1440
attgggggcc gaaatgctga gcctggcctc ttcccgtggc aggccctgat agtggtggag 1500
gacacttcga gagtgccaaa tgacaagtgg tttgggagtg gggccctgct ctctgcgtcc 1560
tggatcctca cagcagctca tgtgctgcgc tcccagcgta gagacaccac ggtgatacca 1620
```

gtctccaagg agcatgtcac cgtctacctg ggcttgcatg atgtgcgaga caaatcgggg 1680
gcagtcaaca gctcagctgc ccgagtggtg ctccacccag acttcaacat ccaaaactac 1740
aaccacgata tagctctggt gcagctgcag gagcctgtgc ccctgggacc ccacgttatg 1800
cctgtctgcc tgccaaggct tgagcctgaa ggcccggccc cccacatgct gggcctggtg 1860
gccggctggg gcatctccaa tcccaatgtg acagtggatg agatcatcag cagtggcaca 1920
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aaaactagct atgagtcccg ctcgggcaat tacagcgtca cggagaacat gttctgtgct 2040
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tttgatgact tgagccagcg ctgggtggtg caaggcctgg tgtcctgggg gggacctgaa 2160
gaatgcggca gcaagcaggt ctatggagtc tacacaaagg tctccaatta cgtggactgg 2220
gtgtgggagc agatgggctt accacaaagt gttgtggagc cccaggtgga acggtgagct 2280
gacttacttc ctcggggcct gcctcccctg agcgaagcta caccgcactt ccgacagcac 2340
actccacatt acttatcaga ccatatggaa tggaacacac tgacctagcg gtggcttctc 2400
ctaccgagac agcccccagg accctgagag gcagagtgtg gtatagggaa aaggctccag 2460
gcaggagacc tgtgttcctg agcttgtcca agtctctttc cctgtctggg cctcactcta 2520
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caggccatgc ttcttacccc agtggccttt attcactcct gaccacttat caaacccatc 2640
ggtcctactg ttggtataac tgagcttgga cctgactatt agaaaatggt ttctaacatt 2700
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tctcttagtg tgatcccttg gagcaccttc atgcctgggg tttctctccc aaaagcttct 2880
tgcagtctaa gccttatccc ttatgttccc cattaaagga atttcaaaag acatggagaa 2940
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cttaaattcc cattgtcaac tcagaacaca tttgggccca tatgccaccc tggaacacca 3060
gctgacacca tgggcgtcca cacctgctgc tccagacaag cacaaagcaa tctttcagcc 3120
ttgaaatgta ttatctgaaa ggctacctga agcccaggcc cgaatatggg gacttagtcg 3180
attacctgga aaaagaaaag acccacactg tgtcctgctg tgcttttggg caggaaaatg 3240
gaagaaagag tggggtgggc acattagaag tcacccaaat cctgccaggc tgcctggcat 3300
ccctggggca tgagctgggc ggagaatcca ccccgcagga tgttcagagg gacccactcc 3360
ttcatttttc agagtcaaag gaatcagagg ctcacccatg gcaggcagtg aaaagagcca 3420
ggagtcctgg gttctagtcc ctgctctgcc cccaactggc tgtataacct ttgaaaaatc 3480
attttctttg tctgagtctc tggttctccg tcagcaacag gctggcataa ggtcccctgc 3540
aggttccttc tagctggagc actcagagct tccctgactg ctagcagcct ctctggccct 3600
cacagggctg attgttctcc ttctccctgg agctctctct cctgaaaatc tccatcagag 3660
caaggcagcc agagaagccc ctgagaggga atgattggga agtgtccact ttctcaaccg 3720
gctcatcaaa cacactcctt tgtctatgaa tggcacatgt aaatgatgtt atattttgta 3780
tcttttatat catatgcttc accattctgt aaagggcctc tgcattgttg ctcccatcag 3840
gggtctcaag tggaaataaa ccctcgtgga taaccaaaaa aaaaaaaaaa aaaaa 3895

<210> 136
<211> 728
<212> PRT
<213> Homo sapiens

<400> 136
Met Arg Trp Leu Leu Leu Tyr Tyr Ala Leu Cys Phe Ser Leu Ser Lys
1 5 10 15
Ala Ser Ala His Thr Val Glu Leu Asn Asn Met Phe Gly Gln Ile Gln
20 25 30
Ser Pro Gly Tyr Pro Asp Ser Tyr Pro Ser Asp Ser Glu Val Thr Trp
35 40 45
Asn Ile Thr Val Pro Asp Gly Phe Arg Ile Lys Leu Tyr Phe Met His
50 55 60
Phe Asn Leu Glu Ser Ser Tyr Leu Cys Glu Tyr Asp Tyr Val Lys Val
65 70 75 80
Glu Thr Glu Asp Gln Val Leu Ala Thr Phe Cys Gly Arg Glu Thr Thr
85 90 95
Asp Thr Glu Gln Thr Pro Gly Gln Glu Val Val Leu Ser Pro Gly Ser

```
                100                 105                 110
Phe Met Ser Ile Thr Phe Arg Ser Asp Phe Ser Asn Glu Glu Arg Phe
            115                 120                 125
Thr Gly Phe Asp Ala His Tyr Met Ala Val Asp Val Asp Glu Cys Lys
        130                 135                 140
Glu Arg Glu Asp Glu Glu Leu Ser Cys Asp His Tyr Cys His Asn Tyr
145                 150                 155                 160
Ile Gly Gly Tyr Tyr Cys Ser Cys Arg Phe Gly Tyr Ile Leu His Thr
                165                 170                 175
Asp Asn Arg Thr Cys Arg Val Glu Cys Ser Asp Asn Leu Phe Thr Gln
            180                 185                 190
Arg Thr Gly Val Ile Thr Ser Pro Asp Phe Pro Asn Pro Tyr Pro Lys
            195                 200                 205
Ser Ser Glu Cys Leu Tyr Thr Ile Glu Leu Glu Glu Gly Phe Met Val
        210                 215                 220
Asn Leu Gln Phe Glu Asp Ile Phe Asp Ile Glu Asp His Pro Glu Val
225                 230                 235                 240
Pro Cys Pro Tyr Asp Tyr Ile Lys Ile Lys Val Gly Pro Lys Val Leu
                245                 250                 255
Gly Pro Phe Cys Gly Glu Lys Ala Pro Glu Pro Ile Ser Thr Gln Ser
            260                 265                 270
His Ser Val Leu Ile Leu Phe His Ser Asp Asn Ser Gly Glu Asn Arg
            275                 280                 285
Gly Trp Arg Leu Ser Tyr Arg Ala Ala Gly Asn Glu Cys Pro Glu Leu
        290                 295                 300
Gln Pro Pro Val His Gly Lys Ile Glu Pro Ser Gln Ala Lys Tyr Phe
305                 310                 315                 320
Phe Lys Asp Gln Val Leu Val Ser Cys Asp Thr Gly Tyr Lys Val Leu
                325                 330                 335
Lys Asp Asn Val Glu Met Asp Thr Phe Gln Ile Glu Cys Leu Lys Asp
            340                 345                 350
Gly Thr Trp Ser Asn Lys Ile Pro Thr Cys Lys Ile Val Asp Cys Arg
            355                 360                 365
Ala Pro Gly Glu Leu Glu His Gly Leu Ile Thr Phe Ser Thr Arg Asn
        370                 375                 380
Asn Leu Thr Thr Tyr Lys Ser Glu Ile Lys Tyr Ser Cys Gln Glu Pro
385                 390                 395                 400
Tyr Tyr Lys Met Leu Asn Asn Asn Thr Gly Ile Tyr Thr Cys Ser Ala
                405                 410                 415
Gln Gly Val Trp Met Asn Lys Val Leu Gly Arg Ser Leu Pro Thr Cys
            420                 425                 430
Leu Pro Glu Cys Gly Gln Pro Ser Arg Ser Leu Pro Ser Leu Val Lys
            435                 440                 445
Arg Ile Ile Gly Gly Arg Asn Ala Glu Pro Gly Leu Phe Pro Trp Gln
        450                 455                 460
Ala Leu Ile Val Val Glu Asp Thr Ser Arg Val Pro Asn Asp Lys Trp
465                 470                 475                 480
Phe Gly Ser Gly Ala Leu Leu Ser Ala Ser Trp Ile Leu Thr Ala Ala
                485                 490                 495
His Val Leu Arg Ser Gln Arg Arg Asp Thr Thr Val Ile Pro Val Ser
            500                 505                 510
Lys Glu His Val Thr Val Tyr Leu Gly Leu His Asp Val Arg Asp Lys
            515                 520                 525
Ser Gly Ala Val Asn Ser Ser Ala Ala Arg Val Val Leu His Pro Asp
        530                 535                 540
Phe Asn Ile Gln Asn Tyr Asn His Asp Ile Ala Leu Val Gln Leu Gln
545                 550                 555                 560
Glu Pro Val Pro Leu Gly Pro His Val Met Pro Val Cys Leu Pro Arg
```

```
                565                 570                 575
Leu Glu Pro Glu Gly Pro Ala Pro His Met Leu Gly Leu Val Ala Gly
            580                 585                 590
Trp Gly Ile Ser Asn Pro Asn Val Thr Val Asp Glu Ile Ile Ser Ser
        595                 600                 605
Gly Thr Arg Thr Leu Ser Asp Val Leu Gln Tyr Val Lys Leu Pro Val
    610                 615                 620
Val Pro His Ala Glu Cys Lys Thr Ser Tyr Glu Ser Arg Ser Gly Asn
625                 630                 635                 640
Tyr Ser Val Thr Glu Asn Met Phe Cys Ala Gly Tyr Tyr Glu Gly Gly
                645                 650                 655
Lys Asp Thr Cys Leu Gly Asp Ser Gly Gly Ala Phe Val Ile Phe Asp
            660                 665                 670
Asp Leu Ser Gln Arg Trp Val Val Gln Gly Leu Val Ser Trp Gly Gly
        675                 680                 685
Pro Glu Glu Cys Gly Ser Lys Gln Val Tyr Gly Val Tyr Thr Lys Val
    690                 695                 700
Ser Asn Tyr Val Asp Trp Val Trp Glu Gln Met Gly Leu Pro Gln Ser
705                 710                 715                 720
Val Val Glu Pro Gln Val Glu Arg
                725
```

<210> 137
<211> 924
<212> DNA
<213> Homo sapiens

<400> 137

```
gcacagcagc aactgactgg gcagcctttc aggaaagatg cagccactcc tgcttctgct 60
ggcctttctc ctacccactg gggctgaggc aggggagatc atcggaggcc gggagagcag 120
gccccactcc cgcccctaca tggcgtatct tcagatccag agtccagcag gtcagagcag 180
atgtggaggg ttcctggtgc gagaagactt tgtgctgaca gcagctcatt gctggggaag 240
caatataaat gtcaccctgg gcgcccacaa tatccagaga cgggaaaaca cccagcaaca 300
catcactgcg cgcagagcca tccgccaccc tcaatataat cagcggacca tccagaatga 360
catcatgtta ttgcagctga gcagaagagt cagacggaat cgaaacgtga acccagtggc 420
tctgcctaga gcccaggagg gactgagacc cgggacgctg tgcactgtgg ccggctgggg 480
cagggtcagc atgaggaggg gaacagatac actccgagag gtgcagctga gagtgcagag 540
ggataggcag tgcctccgca tcttcggttc ctacgacccc cgaaggcaga tttgtgtggg 600
ggaccggcgg gaacggaagg ctgccttcaa gggggattcc ggaggccccc tgctgtgtaa 660
caatgtggcc cacggcatcg tctcctatgg aaagtcgtca ggggttcctc cagaagtctt 720
caccagggtc tcaagtttcc tgccctggat aaggacaaca atgagaagct tcaaactgct 780
ggatcagatg gagacccccc tgtgactgac tcttcttctc ggggacacag gccagctcca 840
cagtgttgcc agagccttaa taaacgtcca cagagtataa ataaccaatt cctcatttgt 900
tcattaaacg tcattcagta ctta                                        924
```

<210> 138
<211> 255
<212> PRT
<213> Homo sapiens

<400> 138

```
Met Gln Pro Leu Leu Leu Leu Leu Ala Phe Leu Leu Pro Thr Gly Ala
 1               5                  10                  15
Glu Ala Gly Glu Ile Ile Gly Gly Arg Glu Ser Arg Pro His Ser Arg
            20                  25                  30
Pro Tyr Met Ala Tyr Leu Gln Ile Gln Ser Pro Ala Gly Gln Ser Arg
        35                  40                  45
```

```
Cys Gly Gly Phe Leu Val Arg Glu Asp Phe Val Leu Thr Ala Ala His
    50                  55                  60
Cys Trp Gly Ser Asn Ile Asn Val Thr Leu Gly Ala His Asn Ile Gln
65                  70                  75                  80
Arg Arg Glu Asn Thr Gln Gln His Ile Thr Ala Arg Arg Ala Ile Arg
                85                  90                  95
His Pro Gln Tyr Asn Gln Arg Thr Ile Gln Asn Asp Ile Met Leu Leu
            100                 105                 110
Gln Leu Ser Arg Arg Val Arg Arg Asn Arg Asn Val Asn Pro Val Ala
        115                 120                 125
Leu Pro Arg Ala Gln Glu Gly Leu Arg Pro Gly Thr Leu Cys Thr Val
    130                 135                 140
Ala Gly Trp Gly Arg Val Ser Met Arg Arg Gly Thr Asp Thr Leu Arg
145                 150                 155                 160
Glu Val Gln Leu Arg Val Gln Arg Asp Arg Gln Cys Leu Arg Ile Phe
                165                 170                 175
Gly Ser Tyr Asp Pro Arg Arg Gln Ile Cys Val Gly Asp Arg Arg Glu
            180                 185                 190
Arg Lys Ala Ala Phe Lys Gly Asp Ser Gly Gly Pro Leu Leu Cys Asn
        195                 200                 205
Asn Val Ala His Gly Ile Val Ser Tyr Gly Lys Ser Ser Gly Val Pro
    210                 215                 220
Pro Glu Val Phe Thr Arg Val Ser Ser Phe Leu Pro Trp Ile Arg Thr
225                 230                 235                 240
Thr Met Arg Ser Phe Lys Leu Leu Asp Gln Met Glu Thr Pro Leu
                245                 250                 255
```

<210> 139
<211> 1001
<212> DNA
<213> Homo sapiens

<400> 139
cgtgggtgca ccctggaccc caccatggct caccggcccc ccagccctgc cctggcgtcc 60
gtgctgctgg ccttgctgct gagcggtgct gcccgagctg cggagatcgt gggcgggcac 120
gaggcgcagc cacactcccg gccctacatg gcctccctgc agatgcgggg gaacccgggc 180
agccacttct gcggaggcac cttgatccac cccagcttcg tgctgacggc cgcgcactgc 240
ctgcgggaca taccccagcg cctggtgaac gtggtgctcg gagcccacaa cgtgcggacg 300
caggagccca cccagcagca cttctcggtg gctcaggtgt ttctgaacaa ctacgacgcg 360
gagaacaaac tgaacgacgt tctcctcatc cagctgagca gcccagccaa cctcagtgcc 420
tccgtcgcca cagtccagct gccacagcag gaccagccag tgccccacgg cacccagtgc 480
ctggccatgg gctggggccg cgtgggtgcc cacgaccccc cagcccaggt cctgcaggag 540
ctcaatgtca ccgtggtcac cttcttctgc cggccacata acatttgcac tttcgtcctt 600
cgccgcaagg ccggcatctg cttcggagac tcaggtggcc ccctgatctg tgatggcatc 660
atccaaggaa tagactcctt cgtgatctgg ggatgtgcca cccgcctttt ccctgacttc 720
ttcacgcggg tagccctcta cgtggactgg atccgttcca cgctgcgccg tgtggaggcc 780
aagggccgcc cctgaaccgc ccctcccaca gcgctggccg ggaccccgag cctggctcca 840
aaccctcgag gcggatcttt ggacagaagc agctcttccc cgaacactgt ggcgtccggg 900
acggccccac ccgtcccccc acactccctc ccacggggct ccgggagaca ggccggccct 960
gcacctcacc ccaccgtgac ctcaataaac gttgaaactc c   1001

<210> 140
<211> 256
<212> PRT
<213> Homo sapiens

<400> 140

```
Met Ala His Arg Pro Pro Ser Pro Ala Leu Ala Ser Val Leu Leu Ala
 1               5                  10                  15
Leu Leu Leu Ser Gly Ala Ala Arg Ala Ala Glu Ile Val Gly Gly His
            20                  25                  30
Glu Ala Gln Pro His Ser Arg Pro Tyr Met Ala Ser Leu Gln Met Arg
        35                  40                  45
Gly Asn Pro Gly Ser His Phe Cys Gly Gly Thr Leu Ile His Pro Ser
    50                  55                  60
Phe Val Leu Thr Ala Ala His Cys Leu Arg Asp Ile Pro Gln Arg Leu
65                  70                  75                  80
Val Asn Val Val Leu Gly Ala His Asn Val Arg Thr Gln Glu Pro Thr
                85                  90                  95
Gln Gln His Phe Ser Val Ala Gln Val Phe Leu Asn Asn Tyr Asp Ala
            100                 105                 110
Glu Asn Lys Leu Asn Asp Val Leu Leu Ile Gln Leu Ser Ser Pro Ala
        115                 120                 125
Asn Leu Ser Ala Ser Val Ala Thr Val Gln Leu Pro Gln Gln Asp Gln
    130                 135                 140
Pro Val Pro His Gly Thr Gln Cys Leu Ala Met Gly Trp Gly Arg Val
145                 150                 155                 160
Gly Ala His Asp Pro Pro Ala Gln Val Leu Gln Glu Leu Asn Val Thr
                165                 170                 175
Val Val Thr Phe Phe Cys Arg Pro His Asn Ile Cys Thr Phe Val Pro
            180                 185                 190
Arg Arg Lys Ala Gly Ile Cys Phe Gly Asp Ser Gly Gly Pro Leu Ile
        195                 200                 205
Cys Asp Gly Ile Ile Gln Gly Ile Asp Ser Phe Val Ile Trp Gly Cys
    210                 215                 220
Ala Thr Arg Leu Phe Pro Asp Phe Phe Thr Arg Val Ala Leu Tyr Val
225                 230                 235                 240
Asp Trp Ile Arg Ser Thr Leu Arg Arg Val Glu Ala Lys Gly Arg Pro
                245                 250                 255
```

<210> 141
<211> 878
<212> DNA
<213> Homo sapiens

<400> 141
cagattttca ggttgattga tgtgggacag cagccacaat gaggaactcc tatagatttc 60
tggcatcctc tctctcagtt gtcgtttctc tcctgctaat tcctgaagat gtctgtgaaa 120
aaattattgg aggaaatgaa gtaactcctc attcaagacc ctacatggtc ctacttagtc 180
ttgacagaaa aaccatctgt gctggggctt tgattgcaaa agactgggtg ttgactgcag 240
ctcactgtaa cttgaacaaa aggtcccagg tcattcttgg ggctcactca ataaccaggg 300
aagagccaac aaaacagata atgcttgtta agaaagagtt tccctatcca tgctatgacc 360
cagccacacg cgaaggtgac cttaaacttt tacagctgac ggaaaaagca aaaattaaca 420
aatatgtgac tatccttcat ctacctaaaa aggggatga tgtgaaacca ggaaccatgt 480
gccaagttgc agggtggggg aggactcaca atagtgcatc ttggtccgat actctgagag 540
aagtcaatat caccatcata gacagaaaag tctgcaatga tcgaaatcac tataatttta 600
accctgtgat tggaatgaat atggtttgtg ctggaagcct ccgaggtgga agagactcgt 660
gcaatggaga ttctggaagc cctttgttgt gcgagggtgt tttccgaggg gtcacttcct 720
ttggccttga aaataaatgc ggagaccctc gtgggcctgg tgtctatatt cttctctcaa 780
agaaacacct caactggata attatgacta tcaagggagc agtttaaata accgtttcct 840
ttcatttact gtggcttctt aatcttttca caaataaa 878

<210> 142
<211> 262

<212> PRT
<213> Homo sapiens

<400> 142

```
Met Arg Asn Ser Tyr Arg Phe Leu Ala Ser Ser Leu Ser Val Val Val
 1               5                  10                  15
Ser Leu Leu Leu Ile Pro Glu Asp Val Cys Glu Lys Ile Ile Gly Gly
            20                  25                  30
Asn Glu Val Thr Pro His Ser Arg Pro Tyr Met Val Leu Leu Ser Leu
        35                  40                  45
Asp Arg Lys Thr Ile Cys Ala Gly Ala Leu Ile Ala Lys Asp Trp Val
    50                  55                  60
Leu Thr Ala Ala His Cys Asn Leu Asn Lys Arg Ser Gln Val Ile Leu
65                  70                  75                  80
Gly Ala His Ser Ile Thr Arg Glu Glu Pro Thr Lys Gln Ile Met Leu
                85                  90                  95
Val Lys Lys Glu Phe Pro Tyr Pro Cys Tyr Asp Pro Ala Thr Arg Glu
            100                 105                 110
Gly Asp Leu Lys Leu Leu Gln Leu Thr Glu Lys Ala Lys Ile Asn Lys
        115                 120                 125
Tyr Val Thr Ile Leu His Leu Pro Lys Lys Gly Asp Asp Val Lys Pro
    130                 135                 140
Gly Thr Met Cys Gln Val Ala Gly Trp Gly Arg Thr His Asn Ser Ala
145                 150                 155                 160
Ser Trp Ser Asp Thr Leu Arg Glu Val Asn Ile Thr Ile Ile Asp Arg
                165                 170                 175
Lys Val Cys Asn Asp Arg Asn His Tyr Asn Phe Asn Pro Val Ile Gly
            180                 185                 190
Met Asn Met Val Cys Ala Gly Ser Leu Arg Gly Gly Arg Asp Ser Cys
        195                 200                 205
Asn Gly Asp Ser Gly Ser Pro Leu Leu Cys Glu Gly Val Phe Arg Gly
    210                 215                 220
Val Thr Ser Phe Gly Leu Glu Asn Lys Cys Gly Asp Pro Arg Gly Pro
225                 230                 235                 240
Gly Val Tyr Ile Leu Leu Ser Lys Lys His Leu Asn Trp Ile Ile Met
                245                 250                 255
Thr Ile Lys Gly Ala Val
            260
```

<210> 143
<211> 947
<212> DNA
<213> Homo sapiens

<400> 143

```
ggctcggggc cggggccagc acccacactg ggtctccaca gcggcatgga ggcctgcgtg 60
tcttcactgc tggtgctggc cctgggggcc ctgtcagtag gcagctcctt tgggacccag 120
atcatcgggg gccgggaggt gatcccccac tcgcgcccgt acatggcctc actgcagaga 180
aatggctccc acctgtgcgg gggtgtcctg gtgcacccaa agtgggtgct gacggctgcc 240
cactgcctgg cccagcggat ggcccagctg aggctggtgc tggggctcca caccctggac 300
agccccggtc tcaccttcca catcaaggca gccatccagc accctcgcta caagcccgtc 360
cctgccctgg agaacgacct cgcgctgctt cagctggacg ggaaagtgaa gcccagccgg 420
accatccggc cgttggccct gcccagtaag cgccaggtgg tggcagcagg gactcggtgc 480
agcatggccg gctgggggct gacccaccag ggcgggcgcc tgtcccgggt gctgcgggag 540
ctggacctcc aagtgctgga cacccgcatg tgtaacaaca gccgcttctg gaacggcagc 600
ctctccccca gcatggtctg cctggcggcc gactccaagg accaggctcc ctgcaagggt 660
gactcgggcg ggcccctggt gtgtggcaaa ggccgggtgt tggccggagt cctgtccttc 720
```

agctccaggg tctgcactga catcttcaag cctcccgtgg ccaccgctgt ggcgccttac 780
gtgtcctgga tcaggaaggt caccggccga tcggcctgat gccctggggt gatggggacc 840
ccctcgctgt ctccacagga cccttcccct ccaggggtgc agtggggtgg gtgaggacgg 900
gtgggaggga cagggaggga ccaataaatc ataatgaaga aacgctc 947

<210> 144
<211> 257
<212> PRT
<213> Homo sapiens

<400> 144
Met Glu Ala Cys Val Ser Ser Leu Leu Val Leu Ala Leu Gly Ala Leu
 1   5   10   15
Ser Val Gly Ser Ser Phe Gly Thr Gln Ile Ile Gly Gly Arg Glu Val
            20   25   30
Ile Pro His Ser Arg Pro Tyr Met Ala Ser Leu Gln Arg Asn Gly Ser
        35   40   45
His Leu Cys Gly Gly Val Leu Val His Pro Lys Trp Val Leu Thr Ala
    50   55   60
Ala His Cys Leu Ala Gln Arg Met Ala Gln Leu Arg Leu Val Leu Gly
65   70   75   80
Leu His Thr Leu Asp Ser Pro Gly Leu Thr Phe His Ile Lys Ala Ala
                85   90   95
Ile Gln His Pro Arg Tyr Lys Pro Val Pro Ala Leu Glu Asn Asp Leu
            100   105   110
Ala Leu Leu Gln Leu Asp Gly Lys Val Lys Pro Ser Arg Thr Ile Arg
        115   120   125
Pro Leu Ala Leu Pro Ser Lys Arg Gln Val Val Ala Ala Gly Thr Arg
    130   135   140
Cys Ser Met Ala Gly Trp Gly Leu Thr His Gln Gly Gly Arg Leu Ser
145   150   155   160
Arg Val Leu Arg Glu Leu Asp Leu Gln Val Leu Asp Thr Arg Met Cys
                165   170   175
Asn Asn Ser Arg Phe Trp Asn Gly Ser Leu Ser Pro Ser Met Val Cys
            180   185   190
Leu Ala Ala Asp Ser Lys Asp Gln Ala Pro Cys Lys Gly Asp Ser Gly
        195   200   205
Gly Pro Leu Val Cys Gly Lys Gly Arg Val Leu Ala Gly Val Leu Ser
    210   215   220
Phe Ser Ser Arg Val Cys Thr Asp Ile Phe Lys Pro Pro Val Ala Thr
225   230   235   240
Ala Val Ala Pro Tyr Val Ser Trp Ile Arg Lys Val Thr Gly Arg Ser
                245   250   255
Ala

<210> 145
<211> 784
<212> DNA
<213> Homo sapiens

<400> 145
agcatttgct caggcagcct ctctgggaag atgctgcttc ttcctctccc cctgctgctc 60
tttctcttgt gctccagagc tgaagctggg gagatcatcg ggggcacaga atgcaagcca 120
cattcccgcc cctacatggc ctacctggaa attgtaactt ccaacggtcc ctcaaaattt 180
tgtggtggtt tccttataag acggaacttt gtgctgacgg ctgctcattg tgcaggaagg 240
tctataacag tcacccttgg agcccataac ataacagagg aagaagacac atggcagaag 300

cttgaggtta taaagcaatt ccgtcatcca aaatataaca cttctactct tcaccacgat 360
atcatgttac taaagttgaa ggagaaagcc agcctgaccc tggctgtggg gacactcccc 420
ttcccatcac aattcaactt tgtcccacct gggagaatgt gccgggtggc tggctgggga 480
agaacaggtg tgttgaagcc gggctcagac actctgcaag aggtgaagct gagactcatg 540
gatccccagg cctgcagcca cttcagagac tttgaccaca atcttcagct gtgtgtgggc 600
aatcccagga agacaaaatc tgcatttaag ggagactctg ggggccctct tctgtgtgct 660
ggggtggccc agggcatcgt atcctatgga cggtcggatg caaagccccc tgctgtcttc 720
acccgaatct cccattaccg gccctggatc aaccagatcc tgcaggcaaa ttaatcctgg 780
atcc 784

<210> 146
<211> 247
<212> PRT
<213> Homo sapiens

<400> 146
Met Leu Leu Leu Pro Leu Pro Leu Leu Leu Phe Leu Leu Cys Ser Arg
1 5 10 15
Ala Glu Ala Gly Glu Ile Ile Gly Gly Thr Glu Cys Lys Pro His Ser
20 25 30
Arg Pro Tyr Met Ala Tyr Leu Glu Ile Val Thr Ser Asn Gly Pro Ser
35 40 45
Lys Phe Cys Gly Gly Phe Leu Ile Arg Arg Asn Phe Val Leu Thr Ala
50 55 60
Ala His Cys Ala Gly Arg Ser Ile Thr Val Thr Leu Gly Ala His Asn
65 70 75 80
Ile Thr Glu Glu Glu Asp Thr Trp Gln Lys Leu Glu Val Ile Lys Gln
85 90 95
Phe Arg His Pro Lys Tyr Asn Thr Ser Thr Leu His His Asp Ile Met
100 105 110
Leu Leu Lys Leu Lys Glu Lys Ala Ser Leu Thr Leu Ala Val Gly Thr
115 120 125
Leu Pro Phe Pro Ser Gln Phe Asn Phe Val Pro Pro Gly Arg Met Cys
130 135 140
Arg Val Ala Gly Trp Gly Arg Thr Gly Val Leu Lys Pro Gly Ser Asp
145 150 155 160
Thr Leu Gln Glu Val Lys Leu Arg Leu Met Asp Pro Gln Ala Cys Ser
165 170 175
His Phe Arg Asp Phe Asp His Asn Leu Gln Leu Cys Val Gly Asn Pro
180 185 190
Arg Lys Thr Lys Ser Ala Phe Lys Gly Asp Ser Gly Gly Pro Leu Leu
195 200 205
Cys Ala Gly Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Ser Asp Ala
210 215 220
Lys Pro Pro Ala Val Phe Thr Arg Ile Ser His Tyr Arg Pro Trp Ile
225 230 235 240
Asn Gln Ile Leu Gln Ala Asn
245

<210> 147
<211> 1194
<212> DNA
<213> Homo sapiens

<400> 147
ataaatgggg aggggagagc ccactgggta gaaggaacag ggagcggcca ggatgctgaa 60
tctgctgctg ctggcgctgc ccgtcctggc gagccgcgcc tacgcggccc ctgccccagg 120

```
ccaggccctg cagcgagtgg gcatcgtcgg gggtcaggag gcccccagga gcaagtggcc 180
ctggcaggtg agcctgagag tccacggccc atactggatg cacttctgcg ggggctccct 240
catccacccc cagtgggtgc tgaccgcagc gcactgcgtg ggaccggacg tcaaggatct 300
ggccgccctc agggtgcaac tgcgggagca gcacctctac taccaggacc agctgctgcc 360
ggtcagcagg atcatcgtgc acccacagtt ctacaccgcc cagatcggag cggacatcgc 420
cctgctggag ctggaggagc cggtgaacgt ctccagccac gtccacacgg tcaccctgcc 480
ccctgcctca gagaccttcc ccccggggat gccgtgctgg gtcactggct ggggcgatgt 540
ggacaatgat gagcgcctcc caccgccatt tcctctgaag caggtgaagg tccccataat 600
ggaaaaccac atttgtgacg caaaatacca ccttggcgcc tacacgggag acgacgtccg 660
catcgtccgt gacgacatgc tgtgtgccgg gaacacccgg agggactcat gccagggcga 720
ctccggaggg cccctggtgt gcaaggtgaa tggcacctgg ctgcaggcgg gcgtggtcag 780
ctggggcgag ggctgtgccc agcccaaccg gcctggcatc tacacccgtg tcacctacta 840
cttggactgg atccaccact atgtccccaa aaagccgtga gtcaggcctg ggttggccac 900
ctgggtcact ggaggaccaa cccctgctgt ccaaaacacc actgcttcct acccaggtgg 960
cgactgcccc ccacaccttc cctgccccgt cctgagtgcc ccttcctgtc ctaagccccc 1020
tgctctcttc tgagcccctt cccctgtcct gaggaccctt ccctatcctg agccccccttc 1080
cctgtcctaa gcctgacgcc tgcaccgggc cctccagccc tcccctgccc agatagctgg 1140
tggtgggcgc taatcctcct gagtgctgga cctcattaaa gtgcatggaa atca        1194
```

<210> 148
<211> 275
<212> PRT
<213> Homo sapiens

<400> 148

```
Met Leu Asn Leu Leu Leu Leu Ala Leu Pro Val Leu Ala Ser Arg Ala
 1               5                  10                  15
Tyr Ala Ala Pro Ala Pro Gly Gln Ala Leu Gln Arg Val Gly Ile Val
            20                  25                  30
Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val Ser Leu
        35                  40                  45
Arg Val His Gly Pro Tyr Trp Met His Phe Cys Gly Gly Ser Leu Ile
    50                  55                  60
His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro Asp Val
65                  70                  75                  80
Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His Leu Tyr
                85                  90                  95
Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His Pro Gln
            100                 105                 110
Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu Leu Glu
        115                 120                 125
Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu Pro Pro
    130                 135                 140
Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr Gly Trp
145                 150                 155                 160
Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro Leu Lys
                165                 170                 175
Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala Lys Tyr
            180                 185                 190
His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg Asp Asp
        195                 200                 205
Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly Asp Ser
    210                 215                 220
Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln Ala Gly
225                 230                 235                 240
Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro Gly Ile
                245                 250                 255
Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr Val Pro
```

```
            260                 265                 270
Lys Lys Pro
        275
```

<210> 149
<211> 1074
<212> DNA
<213> Homo sapiens

<400> 149
gatcaacaca tttcatctgg gcttcttaaa tctaaatctt taaaatgact aagttttctt 60
cctttttctct gtttttccta atagttgggg cttatatgac tcatgtgtgt ttcaatatgg 120
aaattattgg agggaaagaa gtgtcacctc attccaggcc atttatggcc tccatccagt 180
atggcggaca tcacgtttgt ggaggtgttc tgattgatcc acagtgggtg ctgacagcag 240
cccactgcca atatcggttt accaaaggcc agtctcccac tgtggtttta ggcgcacact 300
ctctctcaaa gaatgaggcc tccaaacaaa cactggagat caaaaaattt ataccattct 360
caagagttac atcagatcct caatcaaatg atatcatgct ggttaagctt caaacagccg 420
caaaactcaa taaacatgtc aagatgctcc acataagatc caaaacctct cttagatctg 480
gaaccaaatg caaggttact ggctggggag ccaccgatcc agattcatta agaccttctg 540
acaccctgcg agaagtcact gttactgtcc taagtcgaaa actttgcaac agccaaagtt 600
actacaacgg cgacccttt atcaccaaag acatggtctg tgcaggagat gccaaaggcc 660
agaaggattc ctgtaagggt gactcagggg gcccccttgat ctgtaaaggt gtcttccacg 720
ctatagtctc tggaggtcat gaatgtggtg ttgccacaaa gcctggaatc tacaccctgt 780
taaccaagaa ataccagact tggatcaaaa gcaaccttgt cccgcctcat acaaattaag 840
ttacaaataa ttttattgga tgcacttgct tctttttcc taatatgctc gcaggttaga 900
gttgggtgta agtaaagcag agcacatatg gggtccattt ttgcacttgt aagtcatttt 960
attaaggaat caagttcttt ttcacttgta tcactgatgt atttctacca tgctggtttt 1020
attctaaata aaatttagaa gactcaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1074

<210> 150
<211> 264
<212> PRT
<213> Homo sapiens

<400> 150
```
Met Thr Lys Phe Ser Ser Phe Ser Leu Phe Phe Leu Ile Val Gly Ala
 1               5                  10                  15
Tyr Met Thr His Val Cys Phe Asn Met Glu Ile Ile Gly Gly Lys Glu
            20                  25                  30
Val Ser Pro His Ser Arg Pro Phe Met Ala Ser Ile Gln Tyr Gly Gly
        35                  40                  45
His His Val Cys Gly Gly Val Leu Ile Asp Pro Gln Trp Val Leu Thr
    50                  55                  60
Ala Ala His Cys Gln Tyr Arg Phe Thr Lys Gly Gln Ser Pro Thr Val
65                  70                  75                  80
Val Leu Gly Ala His Ser Leu Ser Lys Asn Glu Ala Ser Lys Gln Thr
                85                  90                  95
Leu Glu Ile Lys Lys Phe Ile Pro Phe Ser Arg Val Thr Ser Asp Pro
            100                 105                 110
Gln Ser Asn Asp Ile Met Leu Val Lys Leu Gln Thr Ala Ala Lys Leu
        115                 120                 125
Asn Lys His Val Lys Met Leu His Ile Arg Ser Lys Thr Ser Leu Arg
    130                 135                 140
Ser Gly Thr Lys Cys Lys Val Thr Gly Trp Gly Ala Thr Asp Pro Asp
145                 150                 155                 160
Ser Leu Arg Pro Ser Asp Thr Leu Arg Glu Val Thr Val Thr Val Leu
                165                 170                 175
```

```
Ser Arg Lys Leu Cys Asn Ser Gln Ser Tyr Tyr Asn Gly Asp Pro Phe
            180                 185                 190
Ile Thr Lys Asp Met Val Cys Ala Gly Asp Ala Lys Gly Gln Lys Asp
        195                 200                 205
Ser Cys Lys Gly Asp Ser Gly Gly Pro Leu Ile Cys Lys Gly Val Phe
    210                 215                 220
His Ala Ile Val Ser Gly Gly His Glu Cys Gly Val Ala Thr Lys Pro
225                 230                 235                 240
Gly Ile Tyr Thr Leu Leu Thr Lys Lys Tyr Gln Thr Trp Ile Lys Ser
                245                 250                 255
Asn Leu Val Pro Pro His Thr Asn
            260
```

<210> 151
<211> 1047
<212> DNA
<213> Homo sapiens

<400> 151
ggagtcaaca ccaacagctc tgacctgggc agccttcctg agaaaatgca gccattcctc 60
ctcctgttgg cctttcttct gacccctggg gctgggacag aggagatcat cgggggccat 120
gaggccaagc cccactcccg cccctacatg gcctttgttc agtttctgca agagaagagt 180
cggaagaggt gtggcggcat cctagtgaga aaggactttg tgctgacagc tgctcactgc 240
cagggaagct ccataaatgt caccttgggg gcccacaata tcaaggaaca ggagcggacc 300
cagcagttta tccctgtgaa aagacccatc ccccatccag cctataatcc taagaacttc 360
tccaacgaca tcatgctact gcagctggag agaaaggcca agtggaccac agctgtgcgg 420
cctctcaggc tacctagcag caaggcccag gtgaagccag ggcagctgtg cagtgtggct 480
ggctggggtt atgtctcaat gagcacttta gcaaccacac tgcaggaagt gttgctgaca 540
gtgcagaagg actgccagtg tgaacgtctc ttccatggca attacagcag agccactgag 600
atttgtgtgg gggatccaaa gaagacacag accggtttca agggggactc cgggggccc 660
ctcgtgtgta aggacgtagc ccaaggtatt ctctcctatg gaaacaaaaa agggacacct 720
ccaggagtct acatcaaggt ctcacacttc ctgccctgga taaagagaac aatgaagcgc 780
ctctaacagc aggcatgaga ctaaccttcc tctgggcctg accatctctg ggacagaggc 840
aagaatcccc aaggggtggg cagtcagggt tgcaggactg taataaatgg atctctggtg 900
tagaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaaa   1047

<210> 152
<211> 246
<212> PRT
<213> Homo sapiens

<400> 152
```
Met Gln Pro Phe Leu Leu Leu Leu Ala Phe Leu Leu Thr Pro Gly Ala
 1               5                  10                  15
Gly Thr Glu Glu Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg
            20                  25                  30
Pro Tyr Met Ala Phe Val Gln Phe Leu Gln Glu Lys Ser Arg Lys Arg
        35                  40                  45
Cys Gly Gly Ile Leu Val Arg Lys Asp Phe Val Leu Thr Ala Ala His
    50                  55                  60
Cys Gln Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys
65                  70                  75                  80
Glu Gln Glu Arg Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro
                85                  90                  95
His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu
```

```
            100                 105                 110
Gln Leu Glu Arg Lys Ala Lys Trp Thr Thr Ala Val Arg Pro Leu Arg
        115                 120                 125
Leu Pro Ser Ser Lys Ala Gln Val Lys Pro Gly Gln Leu Cys Ser Val
    130                 135                 140
Ala Gly Trp Gly Tyr Val Ser Met Ser Thr Leu Ala Thr Thr Leu Gln
145                 150                 155                 160
Glu Val Leu Leu Thr Val Gln Lys Asp Cys Gln Cys Glu Arg Leu Phe
                165                 170                 175
His Gly Asn Tyr Ser Arg Ala Thr Glu Ile Cys Val Gly Asp Pro Lys
            180                 185                 190
Lys Thr Gln Thr Gly Phe Lys Gly Asp Ser Gly Gly Pro Leu Val Cys
        195                 200                 205
Lys Asp Val Ala Gln Gly Ile Leu Ser Tyr Gly Asn Lys Lys Gly Thr
    210                 215                 220
Pro Pro Gly Val Tyr Ile Lys Val Ser His Phe Leu Pro Trp Ile Lys
225                 230                 235                 240
Arg Thr Met Lys Arg Leu
                245
```

<210> 153
<211> 952
<212> DNA
<213> Homo sapiens

<400> 153
ttggtccaag caagaaggca gtggtctact ccatcggcaa catgctggtc ctttatggac 60
acagcaccca ggaccttccg gaaaccaatg cccgcgtagt cggagggact gaggccggga 120
ggaattcctg gccctctcag atttccctcc agtaccggtc tggaggttcc cggtatcaca 180
cctgtggagg gacccttatc agacagaact gggtgatgac agctgctcac tgcgtggatt 240
accagaagac tttccgcgtg gtggctggag accataacct gagccagaat gatggcactg 300
agcagtacgt gagtgtgcag aagatcgtgg tgcatccata ctggaacagc gataacgtgg 360
ctgccggcta tgacatcgcc ctgctgcgcc tggcccagag cgttaccctc aatagctatg 420
tccagctggg tgttctgccc caggagggag ccatcctggc taacaacagt ccctgctaca 480
tcacaggctg gggcaagacc aagaccaatg ggcagctggc ccagaccctg cagcaggctt 540
acctgccctc tgtggactac gccatctgct ccagctcctc ctactggggc tccactgtga 600
agaacaccat ggtgtgtgct ggtggagatg gagttcgctc tggatgccag ggtgactctg 660
ggggcccccc ccattgcttg gtgaatggca agtattctgt ccatggagtg accagctttg 720
tgtccagccg gggctgtaat gtctccagga agcctacagt cttcacccag gtctctgctt 780
acatctcctg gataaataat gtcatcgcct ccaactgaac attttcctga gtccaacgac 840
cttcccaaaa tggttcttag atctgcaata ggacttgcga tcaaaaagta aaacacattc 900
tgaaagacta ttgagccatt gatagaaaag caaataaaac tagatataca tt 952

<210> 154
<211> 258
<212> PRT
<213> Homo sapiens

<400> 154
```
Met Leu Val Leu Tyr Gly His Ser Thr Gln Asp Leu Pro Glu Thr Asn
 1               5                  10                  15
Ala Arg Val Val Gly Gly Thr Glu Ala Gly Arg Asn Ser Trp Pro Ser
            20                  25                  30
Gln Ile Ser Leu Gln Tyr Arg Ser Gly Gly Ser Arg Tyr His Thr Cys
        35                  40                  45
Gly Gly Thr Leu Ile Arg Gln Asn Trp Val Met Thr Ala Ala His Cys
    50                  55                  60
```

```
Val Asp Tyr Gln Lys Thr Phe Arg Val Val Ala Gly Asp His Asn Leu
65                  70                  75                  80
Ser Gln Asn Asp Gly Thr Glu Gln Tyr Val Ser Val Gln Lys Ile Val
                85                  90                  95
Val His Pro Tyr Trp Asn Ser Asp Asn Val Ala Ala Gly Tyr Asp Ile
            100                 105                 110
Ala Leu Leu Arg Leu Ala Gln Ser Val Thr Leu Asn Ser Tyr Val Gln
        115                 120                 125
Leu Gly Val Leu Pro Gln Glu Gly Ala Ile Leu Ala Asn Asn Ser Pro
    130                 135                 140
Cys Tyr Ile Thr Gly Trp Gly Lys Thr Lys Thr Asn Gly Gln Leu Ala
145                 150                 155                 160
Gln Thr Leu Gln Gln Ala Tyr Leu Pro Ser Val Asp Tyr Ala Ile Cys
                165                 170                 175
Ser Ser Ser Ser Tyr Trp Gly Ser Thr Val Lys Asn Thr Met Val Cys
            180                 185                 190
Ala Gly Gly Asp Gly Val Arg Ser Gly Cys Gln Gly Asp Ser Gly Gly
        195                 200                 205
Pro Leu His Cys Leu Val Asn Gly Lys Tyr Ser Val His Gly Val Thr
    210                 215                 220
Ser Phe Val Ser Ser Arg Gly Cys Asn Val Ser Arg Lys Pro Thr Val
225                 230                 235                 240
Phe Thr Gln Val Ser Ala Tyr Ile Ser Trp Ile Asn Asn Val Ile Ala
                245                 250                 255
Ser Asn
```

<210> 155
<211> 963
<212> DNA
<213> Homo sapiens

<400> 155
tcctatcatc acaaaactca tgatgctccg gctgctcagt tccctcctcc ttgtggccgt 60
tgcctcaggc tatggcccac cttcctctca ctcttccagc cgcgttgtcc atggtgagga 120
tgcggtcccc tacagctggc cctggcaggt ttccctgcag tatgagaaaa gtggaagctt 180
ctaccacacg tgtggcggta gcctcatcgc ccccgattgg gttgtgactg ccggccactg 240
catctcgagg gatctgacct accaggtggt gttgggtgag tacaaccttg ctgtgaagga 300
gggccccgag caggtgatcc ccatcaactc tgaggagctg tttgtgcatc cactctggaa 360
ccgctcgtgt gtggcctgtg gcaatgacat cgccctcatc aagctctcac gcagcgccca 420
gctgggagat gccgtccagc tcgcctcact ccctcccgct ggtgacatcc ttcccaacaa 480
gacaccctgc tacatcaccg gctggggccg tctctatacc aatgggccac tcccagacaa 540
gctgcagcag gcccggctgc ccgtggtgga ctataagcac tgctccaggt ggaactggtg 600
gggttccacc gtgaagaaaa ccatggtgtg tgctggaggg tacatccgct ccggctgcaa 660
cggtgactct ggaggacccc tcaactgccc cacagaggat ggtggctggc aggtccacgg 720
tgtgaccagc tttgtttctg gctttggctg caacttcatc tggaagccca cggtgttcac 780
tcgagtctcc gccttcatcg actggattga ggagaccata gcaagccact agaaccaagg 840
cccagctggc agtgctgatc gatcccacat cctgaataaa gaataaagat ctctcagaaa 900
attccaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 960
aaa   963

<210> 156
<211> 270
<212> PRT
<213> Homo sapiens

<400> 156

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Met Met Leu Arg Leu Leu Ser Ser Leu Leu Leu Val Ala Val Ala Ser
 1               5                  10                  15
Gly Tyr Gly Pro Pro Ser Ser His Ser Ser Ser Arg Val Val His Gly
            20                  25                  30
Glu Asp Ala Val Pro Tyr Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
        35                  40                  45
Glu Lys Ser Gly Ser Phe Tyr His Thr Cys Gly Gly Ser Leu Ile Ala
    50                  55                  60
Pro Asp Trp Val Val Thr Ala Gly His Cys Ile Ser Arg Asp Leu Thr
65                  70                  75                  80
Tyr Gln Val Val Leu Gly Glu Tyr Asn Leu Ala Val Lys Glu Gly Pro
                85                  90                  95
Glu Gln Val Ile Pro Ile Asn Ser Glu Glu Leu Phe Val His Pro Leu
            100                 105                 110
Trp Asn Arg Ser Cys Val Ala Cys Gly Asn Asp Ile Ala Leu Ile Lys
        115                 120                 125
Leu Ser Arg Ser Ala Gln Leu Gly Asp Ala Val Gln Leu Ala Ser Leu
    130                 135                 140
Pro Pro Ala Gly Asp Ile Leu Pro Asn Lys Thr Pro Cys Tyr Ile Thr
145                 150                 155                 160
Gly Trp Gly Arg Leu Tyr Thr Asn Gly Pro Leu Pro Asp Lys Leu Gln
                165                 170                 175
Gln Ala Arg Leu Pro Val Val Asp Tyr Lys His Cys Ser Arg Trp Asn
            180                 185                 190
Trp Trp Gly Ser Thr Val Lys Lys Thr Met Val Cys Ala Gly Gly Tyr
        195                 200                 205
Ile Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Pro
    210                 215                 220
Thr Glu Asp Gly Gly Trp Gln Val His Gly Val Thr Ser Phe Val Ser
225                 230                 235                 240
Gly Phe Gly Cys Asn Phe Ile Trp Lys Pro Thr Val Phe Thr Arg Val
                245                 250                 255
Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser His
            260                 265                 270
```

<210> 157
<211> 914
<212> DNA
<213> Homo sapiens

<400> 157

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gtgaagaagc gaggcccaac agctggccct ggcaggtctc cctgcagtac agctccaatg 180
gcaagtggta ccacacctgc ggagggtccc tgatagccaa cagctgggtc ctgacggctg 240
cccactgcat cagctcctcc aggacctacc gcgtggggct gggccggcac aacctctacg 300
ttgcggagtc cggctcgctg gcagtcagtg tctctaagat tgtggtgcac aaggactgga 360
actccaacca aatctccaaa gggaacgaca ttgccctgct caaactggct aaccccgtct 420
ccctcaccga caagatccag ctggcctgcc tccctcctgc cggcaccatt ctacccaaca 480
actacccctg ctacgtcacg ggctggggaa ggctgcagac caacggggct gttcctgatg 540
tcctgcagca gggccggttg ctggttgtgg actatgccac ctgctccagc tctgcctggt 600
ggggcagcag cgtgaaaacc agtatgatct gtgctggggg tgatggcgtg atctccagct 660
gcaacggaga ctctggcggg ccactgaact gtcaggcgtc tgacggccgg tggcaggtgc 720
acggcatcgt cagcttcggg tctcgcctcg gctgcaacta ctaccacaag ccctccgtct 780
tcacgcgggt ctccaattac atcgactgga tcaattcggt gattgcaaat aactaaccaa 840
aagaagtccc tgggactgtt tcagacttgg aaaggtcaca gaaggaaaat aatataataa 900
agtgacaact atgc                                                   914
```

<210> 158
<211> 269
<212> PRT
<213> Homo sapiens

<400> 158

```
Met Ile Arg Thr Leu Leu Leu Ser Thr Leu Val Ala Gly Ala Leu Ser
 1               5                  10                  15
Cys Gly Asp Pro Thr Tyr Pro Pro Tyr Val Thr Arg Val Val Gly Gly
            20                  25                  30
Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
        35                  40                  45
Ser Ser Asn Gly Lys Trp Tyr His Thr Cys Gly Gly Ser Leu Ile Ala
    50                  55                  60
Asn Ser Trp Val Leu Thr Ala Ala His Cys Ile Ser Ser Ser Arg Thr
65                  70                  75                  80
Tyr Arg Val Gly Leu Gly Arg His Asn Leu Tyr Val Ala Glu Ser Gly
                85                  90                  95
Ser Leu Ala Val Ser Val Ser Lys Ile Val Val His Lys Asp Trp Asn
            100                 105                 110
Ser Asn Gln Ile Ser Lys Gly Asn Asp Ile Ala Leu Leu Lys Leu Ala
        115                 120                 125
Asn Pro Val Ser Leu Thr Asp Lys Ile Gln Leu Ala Cys Leu Pro Pro
    130                 135                 140
Ala Gly Thr Ile Leu Pro Asn Asn Tyr Pro Cys Tyr Val Thr Gly Trp
145                 150                 155                 160
Gly Arg Leu Gln Thr Asn Gly Ala Val Pro Asp Val Leu Gln Gln Gly
                165                 170                 175
Arg Leu Leu Val Val Asp Tyr Ala Thr Cys Ser Ser Ser Ala Trp Trp
            180                 185                 190
Gly Ser Ser Val Lys Thr Ser Met Ile Cys Ala Gly Gly Asp Gly Val
        195                 200                 205
Ile Ser Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Gln Ala
    210                 215                 220
Ser Asp Gly Arg Trp Gln Val His Gly Ile Val Ser Phe Gly Ser Arg
225                 230                 235                 240
Leu Gly Cys Asn Tyr Tyr His Lys Pro Ser Val Phe Thr Arg Val Ser
                245                 250                 255
Asn Tyr Ile Asp Trp Ile Asn Ser Val Ile Ala Asn Asn
            260                 265
```

<210> 159
<211> 3696
<212> DNA
<213> Homo sapiens

<400> 159

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accagacagt tcttaaatta gcaagccttc aaaaccaaaa atggggtcga aaagaggcat 60
atcttctagg catcattctc tcagctccta tgaaatcatg tttgcagctc tctttgccat 120
attggtagtg ctctgtgctg gattaattgc agtatcctgc ctgacaatca aggaatccca 180
acgaggtgca gcacttggac agagtcatga agccagagcg acatttaaaa taacatccgg 240
agttacatat aatcctaatt tgcaagacaa actctcagtg gatttcaaag ttcttgcttt 300
tgaccttcag caaatgatag atgagatctt tctatcaagc aatctgaaga atgaatataa 360
gaactcaaga gttttacaat ttgaaaatgg cagcattata gtcgtatttg acctttttctt 420
tgcccagtgg gtgtcagatc aaaatgtaaa agaagaactg attcaaggcc ttgaagcaaa 480
taaatccagc caactggtca ctttccatat tgatttgaac agcgttgata tcctagacaa 540
```

gctaacaacc accagtcatc tggcaactcc aggaaatgtc tcaatagagt gcctgcctgg 600
ttcaagtcct tgtactgatg ctctaacgtg tataaaagct gatttatttt gtgatggaga 660
agtaaactgt ccagatggtt ctgacgaaga caataaaatg tgtgccacag tttgtgatgg 720
aagatttttg ttaactggat catctgggtc tttccaggct actcattatc caaaaccttc 780
tgaaacaagt gttgtctgcc agtggatcat acgtgtaaac caaggacttt ccattaaact 840
gagcttcgat gattttaata catattatac agatatatta gatatttatg aaggtgtagg 900
atcaagcaag attttaagag cttctatttg ggaaactaat cctggcacaa taagaatttt 960
ttccaaccaa gttactgcca cctttcttat agaatctgat gaaagtgatt atgttggctt 1020
taatgcaaca tatactgcat ttaacagcag tgagcttaat aattatgaga aaattaattg 1080
taactttgag gatggctttt gtttctgggt ccaggatcta aatgatgata atgaatggga 1140
aaggattcag ggaagcacct tttctccttt tactggaccc aattttgacc acacttttgg 1200
caatgcttca ggattttaca tttctacccc aactggacca ggagggagac aagaacgagt 1260
ggggctttta agcctccctt tggaccccac tttggagcca gcttgcctta gtttctggta 1320
tcatatgtat ggtgaaaatg tccataaatt aagcattaat atcagcaatg accaaaatat 1380
ggagaagaca gttttccaaa aggaaggaaa ttatggagac aattggaatt atggacaagt 1440
aaccctaaat gaaacagtta aatttaaggt tgcttttaat gcttttaaaa acaagatcct 1500
gagtgatatt gcgttggatg acattagcct aacatatggg atttgcaatg ggagtcttta 1560
tccagaacca actttggtgc caactcctcc accagaactt cctacggact gtggaggacc 1620
ttttgagctg tgggagccaa atacaacatt cagttctacg aactttccaa acagctaccc 1680
taatctggct ttctgtgttt ggattttaaa tgcacaaaaa ggaaagaata tacaacttca 1740
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taccaccaac agaatgactg tgcttctcat cactaacgat gtgttggcaa gaggagggtt 1920
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ttttcaatgt aaaaatggag agtgtgttcc actggtgaat ctctgtgacg gtcatctgca 2040
ctgtgaggat ggctcagatg aagcagattg tgtgcgtttt ttcaatggca caacgaacaa 2100
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gaccacccag atttcaaatg atgtttgtca actgctggga ctagggagtg gaaactcatc 2220
aaagccaatc ttctctaccg atggtggacc atttgtcaaa ttaaacacag cacctgatgg 2280
ccacttaata ctaacaccca gtcaacagtg tttacaggat tccttgattc ggttacagtg 2340
taaccataaa tcttgtggaa aaaaactggc agctcaagac atcaccccaa agattgttgg 2400
aggaagtaat gccaaagaag gggcctggcc ctgggttgtg ggtctgtatt atggcggccg 2460
actgctctgc ggcgcatctc tcgtcagcag tgactggctg gtgtccgccg cacactgcgt 2520
gtatgggaga aacttagagc catccaagtg gacagcaatc ctaggcctgc atatgaaatc 2580
aaatctgacc tctcctcaaa cagtccctcg attaatagat gaaattgtca taaaccctca 2640
ttacaatagg cgaagaaagg acaacgacat tgccatgatg catctggaat ttaaagtgaa 2700
ttacacagat tacatacaac ctatttgttt accggaagaa aatcaagttt ttcctccagg 2760
aagaaattgt tctattgctg gttgggggac ggttgtatat caaggtacta ctgcaaacat 2820
attgcaagaa gctgatgttc ctcttctatc aaatgagaga tgccaacagc agatgccaga 2880
atataacatt actgaaaata tgatatgtgc aggctatgaa gaaggaggaa tagattcttg 2940
tcaggggat tcaggaggac cattaatgtg ccaagaaaac aacaggtggt tccttgctgg 3000
tgtgacctca tttggataca agtgtgccct gcctaatcgc cccggagtgt atgccagggt 3060
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ggaaagtcgc attatttcc cattctactc tagaaagcat ggaaattaag tgtttcgtac 3180
aaaaatttta aaaagttacc aaaggttttt attcttacct atgtcaatga aatgctaggg 3240
ggccagggaa acaaaatttt aaaaataata aaattcacca tagcaataca gaataacttt 3300
aaaataccat taaatacatt tgtatttcat tgtgaacagg tatttcttca cagatctcat 3360
ttttaaaatt cttaatgatt atttttatta cttactgttg tttaaaggga tgttatttta 3420
aagcatatac catacactta agaaatttga gcagaattta aaaaagaaag aaaataaatt 3480
gtttttccca aagtatgtca ctgttggaaa taaactgcca taaatttttct agttccagtt 3540
tagtttgctg ctattagcag aaactcaatt gtttctctgt cttttctatc aaaattttca 3600
acatatgcat aaccttagta ttttcccaac caatagaaac tatttattgt aagcttatgt 3660
cacaggcctg gactaaattg attttacgtt cctctt 3696

<210> 160
<211> 1019
<212> PRT
<213> Homo sapiens

<400> 160

```
Met Gly Ser Lys Arg Gly Ile Ser Ser Arg His His Ser Leu Ser Ser
 1               5                  10                  15
Tyr Glu Ile Met Phe Ala Ala Leu Phe Ala Ile Leu Val Val Leu Cys
            20                  25                  30
Ala Gly Leu Ile Ala Val Ser Cys Leu Thr Ile Lys Glu Ser Gln Arg
        35                  40                  45
Gly Ala Ala Leu Gly Gln Ser His Glu Ala Arg Ala Thr Phe Lys Ile
    50                  55                  60
Thr Ser Gly Val Thr Tyr Asn Pro Asn Leu Gln Asp Lys Leu Ser Val
65                  70                  75                  80
Asp Phe Lys Val Leu Ala Phe Asp Leu Gln Gln Met Ile Asp Glu Ile
                85                  90                  95
Phe Leu Ser Ser Asn Leu Lys Asn Glu Tyr Lys Asn Ser Arg Val Leu
            100                 105                 110
Gln Phe Glu Asn Gly Ser Ile Ile Val Val Phe Asp Leu Phe Phe Ala
        115                 120                 125
Gln Trp Val Ser Asp Gln Asn Val Lys Glu Glu Leu Ile Gln Gly Leu
    130                 135                 140
Glu Ala Asn Lys Ser Ser Gln Leu Val Thr Phe His Ile Asp Leu Asn
145                 150                 155                 160
Ser Val Asp Ile Leu Asp Lys Leu Thr Thr Thr Ser His Leu Ala Thr
                165                 170                 175
Pro Gly Asn Val Ser Ile Glu Cys Leu Pro Gly Ser Ser Pro Cys Thr
            180                 185                 190
Asp Ala Leu Thr Cys Ile Lys Ala Asp Leu Phe Cys Asp Gly Glu Val
        195                 200                 205
Asn Cys Pro Asp Gly Ser Asp Glu Asp Asn Lys Met Cys Ala Thr Val
    210                 215                 220
Cys Asp Gly Arg Phe Leu Leu Thr Gly Ser Ser Gly Ser Phe Gln Ala
225                 230                 235                 240
Thr His Tyr Pro Lys Pro Ser Glu Thr Ser Val Val Cys Gln Trp Ile
                245                 250                 255
Ile Arg Val Asn Gln Gly Leu Ser Ile Lys Leu Ser Phe Asp Asp Phe
            260                 265                 270
Asn Thr Tyr Tyr Thr Asp Ile Leu Asp Ile Tyr Glu Gly Val Gly Ser
        275                 280                 285
Ser Lys Ile Leu Arg Ala Ser Ile Trp Glu Thr Asn Pro Gly Thr Ile
    290                 295                 300
Arg Ile Phe Ser Asn Gln Val Thr Ala Thr Phe Leu Ile Glu Ser Asp
305                 310                 315                 320
Glu Ser Asp Tyr Val Gly Phe Asn Ala Thr Tyr Thr Ala Phe Asn Ser
                325                 330                 335
Ser Glu Leu Asn Asn Tyr Glu Lys Ile Asn Cys Asn Phe Glu Asp Gly
            340                 345                 350
Phe Cys Phe Trp Val Gln Asp Leu Asn Asp Asp Asn Glu Trp Glu Arg
        355                 360                 365
Ile Gln Gly Ser Thr Phe Ser Pro Phe Thr Gly Pro Asn Phe Asp His
    370                 375                 380
Thr Phe Gly Asn Ala Ser Gly Phe Tyr Ile Ser Thr Pro Thr Gly Pro
385                 390                 395                 400
Gly Gly Arg Gln Glu Arg Val Gly Leu Leu Ser Leu Pro Leu Asp Pro
                405                 410                 415
Thr Leu Glu Pro Ala Cys Leu Ser Phe Trp Tyr His Met Tyr Gly Glu
            420                 425                 430
Asn Val His Lys Leu Ser Ile Asn Ile Ser Asn Asp Gln Asn Met Glu
        435                 440                 445
```

```
Lys Thr Val Phe Gln Lys Glu Gly Asn Tyr Gly Asp Asn Trp Asn Tyr
    450                 455                 460
Gly Gln Val Thr Leu Asn Glu Thr Val Lys Phe Lys Val Ala Phe Asn
465                 470                 475                 480
Ala Phe Lys Asn Lys Ile Leu Ser Asp Ile Ala Leu Asp Asp Ile Ser
                485                 490                 495
Leu Thr Tyr Gly Ile Cys Asn Gly Ser Leu Tyr Pro Glu Pro Thr Leu
            500                 505                 510
Val Pro Thr Pro Pro Pro Glu Leu Pro Thr Asp Cys Gly Gly Pro Phe
        515                 520                 525
Glu Leu Trp Glu Pro Asn Thr Thr Phe Ser Ser Thr Asn Phe Pro Asn
    530                 535                 540
Ser Tyr Pro Asn Leu Ala Phe Cys Val Trp Ile Leu Asn Ala Gln Lys
545                 550                 555                 560
Gly Lys Asn Ile Gln Leu His Phe Gln Glu Phe Asp Leu Glu Asn Ile
                565                 570                 575
Asn Asp Val Val Glu Ile Arg Asp Gly Glu Glu Ala Asp Ser Leu Leu
            580                 585                 590
Leu Ala Val Tyr Thr Gly Pro Gly Pro Val Lys Asp Val Phe Ser Thr
        595                 600                 605
Thr Asn Arg Met Thr Val Leu Leu Ile Thr Asn Asp Val Leu Ala Arg
    610                 615                 620
Gly Gly Phe Lys Ala Asn Phe Thr Thr Gly Tyr His Leu Gly Ile Pro
625                 630                 635                 640
Glu Pro Cys Lys Ala Asp His Phe Gln Cys Lys Asn Gly Glu Cys Val
                645                 650                 655
Pro Leu Val Asn Leu Cys Asp Gly His Leu His Cys Glu Asp Gly Ser
            660                 665                 670
Asp Glu Ala Asp Cys Val Arg Phe Phe Asn Gly Thr Thr Asn Asn Asn
        675                 680                 685
Gly Leu Val Arg Phe Arg Ile Gln Ser Ile Trp His Thr Ala Cys Ala
    690                 695                 700
Glu Asn Trp Thr Thr Gln Ile Ser Asn Asp Val Cys Gln Leu Leu Gly
705                 710                 715                 720
Leu Gly Ser Gly Asn Ser Ser Lys Pro Ile Phe Ser Thr Asp Gly Gly
                725                 730                 735
Pro Phe Val Lys Leu Asn Thr Ala Pro Asp Gly His Leu Ile Leu Thr
            740                 745                 750
Pro Ser Gln Gln Cys Leu Gln Asp Ser Leu Ile Arg Leu Gln Cys Asn
        755                 760                 765
His Lys Ser Cys Gly Lys Lys Leu Ala Ala Gln Asp Ile Thr Pro Lys
    770                 775                 780
Ile Val Gly Gly Ser Asn Ala Lys Glu Gly Ala Trp Pro Trp Val Val
785                 790                 795                 800
Gly Leu Tyr Tyr Gly Gly Arg Leu Leu Cys Gly Ala Ser Leu Val Ser
                805                 810                 815
Ser Asp Trp Leu Val Ser Ala Ala His Cys Val Tyr Gly Arg Asn Leu
            820                 825                 830
Glu Pro Ser Lys Trp Thr Ala Ile Leu Gly Leu His Met Lys Ser Asn
        835                 840                 845
Leu Thr Ser Pro Gln Thr Val Pro Arg Leu Ile Asp Glu Ile Val Ile
    850                 855                 860
Asn Pro His Tyr Asn Arg Arg Arg Lys Asp Asn Asp Ile Ala Met Met
865                 870                 875                 880
His Leu Glu Phe Lys Val Asn Tyr Thr Asp Tyr Ile Gln Pro Ile Cys
                885                 890                 895
Leu Pro Glu Glu Asn Gln Val Phe Pro Pro Gly Arg Asn Cys Ser Ile
            900                 905                 910
```

```
Ala Gly Trp Gly Thr Val Val Tyr Gln Gly Thr Thr Ala Asn Ile Leu
        915                 920                 925
Gln Glu Ala Asp Val Pro Leu Leu Ser Asn Glu Arg Cys Gln Gln Gln
    930                 935                 940
Met Pro Glu Tyr Asn Ile Thr Glu Asn Met Ile Cys Ala Gly Tyr Glu
945                 950                 955                 960
Glu Gly Gly Ile Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Met
                965                 970                 975
Cys Gln Glu Asn Asn Arg Trp Phe Leu Ala Gly Val Thr Ser Phe Gly
            980                 985                 990
Tyr Lys Cys Ala Leu Pro Asn Arg Pro Gly Val Tyr Ala Arg Val Ser
        995                 1000                1005
Arg Phe Thr Glu Trp Ile Gln Ser Phe Leu His
    1010                1015
```

<210> 161
<211> 917
<212> DNA
<213> Homo sapiens

<400> 161

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cagccagtcc tgagcaccta accatgttgg gcatcactgt cctcgctgcg ctcttggcct 60
gtgcctccag ctgtggggtg cccagcttcc cgcccaacct atccgcccga gtggtgggag 120
gagaggatgc ccggccccac agctggccct ggcagatctc cctccagtac ctcaagaacg 180
acacgtggag gcatacgtgt ggcgggactt tgattgctag caacttcgtc ctcactgccg 240
cccactgcat cagcaacacc cggacctacc gtgtggccgt gggaaagaac aacctggagg 300
tggaagacga agaaggatcc ctgtttgtgg gtgtggacac catccacgtc cacaagagat 360
ggaatgccct cctgttgcgc aatgatattg ccctcatcaa gcttgcagag catgtggagc 420
tgagtgacac catccaggtg gcctgcctgc cagagaagga ctccctgctc cccaaggact 480
acccctgcta tgtcaccggc tggggccgcc tctggaccaa cggccccatt gctgataagc 540
tgcagcaggg cctgcagccc gtggtggatc acgccacgtg ctccaggatt gactggtggg 600
gcttcagggt gaagaaaacc atggtgtgcg ctgggggcga tggcgtcatc tcagcctgca 660
atggggactc cggtggccca ctgaactgcc agttggagaa cggttcctgg gaggtgtttg 720
gcatcgtcag ctttggctcc cggcggggct gcaacacccg caagaagccg gtagtctaca 780
cccgggtgtc cgcctacatc gactggatca acgagaaaat gcagctgtga tttgttgctg 840
ggagcggcgg cagcgagtcc ctgcaacagc aataaacttc cttctcctcg ggccacctga 900
aaaaaaaaaa aaaaaaa                                                 917
```

<210> 162
<211> 268
<212> PRT
<213> Homo sapiens

<400> 162

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Met Leu Gly Ile Thr Val Leu Ala Ala Leu Leu Ala Cys Ala Ser Ser
 1               5                  10                  15
Cys Gly Val Pro Ser Phe Pro Pro Asn Leu Ser Ala Arg Val Val Gly
            20                  25                  30
Gly Glu Asp Ala Arg Pro His Ser Trp Pro Trp Gln Ile Ser Leu Gln
        35                  40                  45
Tyr Leu Lys Asn Asp Thr Trp Arg His Thr Cys Gly Gly Thr Leu Ile
    50                  55                  60
Ala Ser Asn Phe Val Leu Thr Ala Ala His Cys Ile Ser Asn Thr Arg
65                  70                  75                  80
Thr Tyr Arg Val Ala Val Gly Lys Asn Asn Leu Glu Val Glu Asp Glu
                85                  90                  95
Glu Gly Ser Leu Phe Val Gly Val Asp Thr Ile His Val His Lys Arg
```

```
                100                 105                 110
Trp Asn Ala Leu Leu Leu Arg Asn Asp Ile Ala Leu Ile Lys Leu Ala
        115                 120                 125
Glu His Val Glu Leu Ser Asp Thr Ile Gln Val Ala Cys Leu Pro Glu
    130                 135                 140
Lys Asp Ser Leu Leu Pro Lys Asp Tyr Pro Cys Tyr Val Thr Gly Trp
145                 150                 155                 160
Gly Arg Leu Trp Thr Asn Gly Pro Ile Ala Asp Lys Leu Gln Gln Gly
                165                 170                 175
Leu Gln Pro Val Val Asp His Ala Thr Cys Ser Arg Ile Asp Trp Trp
            180                 185                 190
Gly Phe Arg Val Lys Lys Thr Met Val Cys Ala Gly Gly Asp Gly Val
        195                 200                 205
Ile Ser Ala Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Gln Leu
    210                 215                 220
Glu Asn Gly Ser Trp Glu Val Phe Gly Ile Val Ser Phe Gly Ser Arg
225                 230                 235                 240
Arg Gly Cys Asn Thr Arg Lys Lys Pro Val Val Tyr Thr Arg Val Ser
                245                 250                 255
Ala Tyr Ile Asp Trp Ile Asn Glu Lys Met Gln Leu
            260                 265
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<210> 163
<211> 1938
<212> DNA
<213> Homo sapoens

<400> 163

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gactttggtg gcaagaggag ctggcggagc ccagccagtg ggcggggcca ggggaggggc 60
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cgtccacact gctcgcttcg gatactccag gcgtctcccg ttgcggccgc tccctgcctt 180
agaggccagc cttggacact tgctgccccc ttccagcccg gattctggga tccttccctc 240
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cggaaggggc agaagctccc tgcggtgtgg ccccccaagc acgcatcaca ggtggcagca 480
gtgcagtcgc cggtcagtgg ccctggcagg tcagcatcac ctatgaaggc gtccatgtgt 540
gtggtggctc tctcgtgtct gagcagtggg tgctgtcagc tgctcactgc ttccccagcg 600
agcaccacaa ggaagcctat gaggtcaagc tgggggccca ccagctagac tcctactccg 660
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tccggcccat ctgcctccct gcagccaacg cctccttccc caacggcctc cactgcactg 840
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aactcgaggt gcctctgatc agtcgtgaga cgtgtaactg cctgtacaac atcgacgcca 960
agcctgagga gccgcacttt gtccaagagg acatggtgtg tgctggctat gtggaggggg 1020
gcaaggacgc ctgccagggt gactctgggg gcccactctc ctgccctgtg gagggtctct 1080
ggtacctgac gggcattgtg agctggggag atgcctgtgg ggcccgcaac aggcctggtg 1140
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ctcgtgtggt gccccaaacc caggagtccc agcccgacag caacctctgt ggcagccacc 1260
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attaaaatgt ttgagcac 1938

<210> 164
<211> 343
<212> PRT
<213> Homo sapiens

<400> 164

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Ile	Leu	Leu	Tyr	Leu	Gly	Leu	Leu	Arg	Ser	Gly	Thr	Gly	Ala	Glu	Gly
			20					25					30		
Ala	Glu	Ala	Pro	Cys	Gly	Val	Ala	Pro	Gln	Ala	Arg	Ile	Thr	Gly	Gly
		35					40					45			
Ser	Ser	Ala	Val	Ala	Gly	Gln	Trp	Pro	Trp	Gln	Val	Ser	Ile	Thr	Tyr
	50					55					60				
Glu	Gly	Val	His	Val	Cys	Gly	Gly	Ser	Leu	Val	Ser	Glu	Gln	Trp	Val
65					70					75					80
Leu	Ser	Ala	Ala	His	Cys	Phe	Pro	Ser	Glu	His	His	Lys	Glu	Ala	Tyr
				85					90					95	
Glu	Val	Lys	Leu	Gly	Ala	His	Gln	Leu	Asp	Ser	Tyr	Ser	Glu	Asp	Ala
			100					105					110		
Lys	Val	Ser	Thr	Leu	Lys	Asp	Ile	Ile	Pro	His	Pro	Ser	Tyr	Leu	Gln
		115					120					125			
Glu	Gly	Ser	Gln	Gly	Asp	Ile	Ala	Leu	Leu	Gln	Leu	Ser	Arg	Pro	Ile
	130					135					140				
Thr	Phe	Ser	Arg	Tyr	Ile	Arg	Pro	Ile	Cys	Leu	Pro	Ala	Ala	Asn	Ala
145					150					155					160
Ser	Phe	Pro	Asn	Gly	Leu	His	Cys	Thr	Val	Thr	Gly	Trp	Gly	His	Val
				165					170					175	
Ala	Pro	Ser	Val	Ser	Leu	Leu	Thr	Pro	Lys	Pro	Leu	Gln	Gln	Leu	Glu
			180					185					190		
Val	Pro	Leu	Ile	Ser	Arg	Glu	Thr	Cys	Asn	Cys	Leu	Tyr	Asn	Ile	Asp
		195					200					205			
Ala	Lys	Pro	Glu	Glu	Pro	His	Phe	Val	Gln	Glu	Asp	Met	Val	Cys	Ala
	210					215					220				
Gly	Tyr	Val	Glu	Gly	Gly	Lys	Asp	Ala	Cys	Gln	Gly	Asp	Ser	Gly	Gly
225					230					235					240
Pro	Leu	Ser	Cys	Pro	Val	Glu	Gly	Leu	Trp	Tyr	Leu	Thr	Gly	Ile	Val
				245					250					255	
Ser	Trp	Gly	Asp	Ala	Cys	Gly	Ala	Arg	Asn	Arg	Pro	Gly	Val	Tyr	Thr
			260					265					270		
Leu	Ala	Ser	Ser	Tyr	Ala	Ser	Trp	Ile	Gln	Ser	Lys	Val	Thr	Glu	Leu
		275					280					285			
Gln	Pro	Arg	Val	Val	Pro	Gln	Thr	Gln	Glu	Ser	Gln	Pro	Asp	Ser	Asn
	290					295					300				
Leu	Cys	Gly	Ser	His	Leu	Ala	Phe	Ser	Ser	Ala	Pro	Ala	Gln	Gly	Leu
305					310					315					320
Leu	Arg	Pro	Ile	Leu	Phe	Leu	Pro	Leu	Gly	Leu	Ala	Leu	Gly	Leu	Leu
				325					330					335	
Ser	Pro	Trp	Leu	Ser	Glu	His									
			340												

<210> 165

<211> 874
<212> DNA
<213> Homo sapiens

<400> 165
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cagtttgttc atgtcagtga gagcttccca caccctggct tcaacatgag cctcctggag 360
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gagcctgctg ataccatcac agatgctgtg aaggtcgtgg agttgcccac cgaggaaccc 480
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<210> 166
<211> 262
<212> PRT
<213> Homo sapiens

<400> 166
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Ala Ala Pro Pro Ile Gln Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
            20   25   30
Gln His Ser Gln Pro Trp Gln Ala Ala Leu Tyr His Phe Ser Thr Phe
        35   40   45
Gln Cys Gly Gly Ile Leu Val His Arg Gln Trp Val Leu Thr Ala Ala
    50   55   60
His Cys Ile Ser Asp Asn Tyr Gln Leu Trp Leu Gly Arg His Asn Leu
65   70   75   80
Phe Asp Asp Glu Asn Thr Ala Gln Phe Val His Val Ser Glu Ser Phe
                85   90   95
Pro His Pro Gly Phe Asn Met Ser Leu Leu Glu Asn His Thr Arg Gln
            100   105   110
Ala Asp Glu Asp Tyr Ser His Asp Leu Met Leu Leu Arg Leu Thr Glu
        115   120   125
Pro Ala Asp Thr Ile Thr Asp Ala Val Lys Val Val Glu Leu Pro Thr
    130   135   140
Glu Glu Pro Glu Val Gly Ser Thr Cys Leu Ala Ser Gly Trp Gly Ser
145   150   155   160
Ile Glu Pro Glu Asn Phe Ser Phe Pro Asp Asp Leu Gln Cys Val Asp
                165   170   175
Leu Lys Ile Leu Pro Asn Asp Glu Cys Lys Lys Ala His Val Gln Lys
            180   185   190
Val Thr Asp Phe Met Leu Cys Val Gly His Leu Glu Gly Gly Lys Asp
        195   200   205
Thr Cys Val Gly Asp Ser Gly Gly Pro Leu Met Cys Asp Gly Val Leu
    210   215   220
Gln Gly Val Thr Ser Trp Gly Tyr Val Pro Cys Gly Thr Pro Asn Lys
225   230   235   240
Pro Ser Val Ala Val Arg Val Leu Ser Tyr Val Lys Trp Ile Glu Asp

245 250 255
Thr Ile Ala Glu Asn Ser
260

<210> 167
<211> 2855
<212> DNA
<213> Homo sapiens

<400> 167
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gaggctggga gtgtgagaag cattcccaac cctggcaggt ggctgtgtac agtcatggat 180
gggcacactg tgggggtgtc ctggtgcacc cccagtgggt gctcacagct gcccattgcc 240
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<210> 168
<211> 261
<212> PRT
<213> Homo sapiens

<400> 168
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Ala Val Pro Leu Ile Gln Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
20 25 30
Lys His Ser Gln Pro Trp Gln Val Ala Val Tyr Ser His Gly Trp Ala
35 40 45
His Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
50 55 60
His Cys Leu Lys Lys Asn Ser Gln Val Trp Leu Gly Arg His Asn Leu
65 70 75 80
Phe Glu Pro Glu Asp Thr Gly Gln Arg Val Pro Val Ser His Ser Phe
85 90 95
Pro His Pro Leu Tyr Asn Met Ser Leu Leu Lys His Gln Ser Leu Arg
100 105 110
Pro Asp Glu Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu
115 120 125
Pro Ala Lys Ile Thr Asp Val Val Lys Val Leu Gly Leu Pro Thr Gln
130 135 140
Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile
145 150 155 160
Glu Pro Glu Glu Phe Leu Arg Pro Arg Ser Leu Gln Cys Val Ser Leu
165 170 175
His Leu Leu Ser Asn Asp Met Cys Ala Arg Ala Tyr Ser Glu Lys Val
180 185 190
Thr Glu Phe Met Leu Cys Ala Gly Leu Trp Thr Gly Gly Lys Asp Thr
195 200 205
Cys Gly Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Gly Val Leu Gln
210 215 220
Gly Ile Thr Ser Trp Gly Pro Glu Pro Cys Ala Leu Pro Glu Lys Pro
225 230 235 240
Ala Val Tyr Thr Lys Val Val His Tyr Arg Lys Trp Ile Lys Asp Thr
245 250 255
Ile Ala Ala Asn Pro
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<210> 169
<211> 2892
<212> DNA
<213> Homo sapiens

<400> 169
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<210> 170
<211> 223
<212> PRT
<213> Homo sapiens

<400> 170

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Ala Val Pro Leu Ile Gln Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
            20                  25                  30
Lys His Ser Gln Pro Trp Gln Val Ala Val Tyr Ser His Gly Trp Ala
        35                  40                  45
His Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
    50                  55                  60
His Cys Leu Lys Lys Asn Ser Gln Val Trp Leu Gly Arg His Asn Leu
65                  70                  75                  80
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Phe Glu Pro Glu Asp Thr Gly Gln Arg Val Pro Val Ser His Ser Phe
                85                  90                  95
Pro His Pro Leu Tyr Asn Met Ser Leu Leu Lys His Gln Ser Leu Arg
            100                 105                 110
Pro Asp Glu Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu
        115                 120                 125
Pro Ala Lys Ile Thr Asp Val Val Lys Val Leu Gly Leu Pro Thr Gln
    130                 135                 140
Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile
145                 150                 155                 160
Glu Pro Glu Glu Phe Leu Arg Pro Arg Ser Leu Gln Cys Val Ser Leu
                165                 170                 175
His Leu Leu Ser Asn Asp Met Cys Ala Arg Ala Tyr Ser Glu Lys Val
            180                 185                 190
Thr Glu Phe Met Leu Cys Ala Gly Leu Trp Thr Gly Gly Lys Asp Thr
        195                 200                 205
Cys Gly Val Ser His Pro Tyr Ser Gln His Leu Glu Gly Lys Gly
    210                 215                 220
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<210> 171
<211> 2879
<212> DNA
<213> Homo sapiens

<400> 171

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tacggacagc atataattct ccctgcaagg atgtatgata atatgtacaa agtaattcca 1860
actgaggaag ctcacctgat ccttagtgtc caaggttttt actgggggtc tgtaggacga 1920
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gtatggagta cttgaataat tgacctgaag tcctcagacc tgaggttccc tagagttcaa 1980
acagatacag catggtccag agtcccagat gtacaaaaac agggattcat cacaaatccc 2040
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agaacatgcc aaggaatcaa atgtcatctc ccaggagtta ttcaagggtg agcccctttac 2160
ttgggatgta caggctttga gcagtgcagg gctgctgagt caaccttta ttgtacaggg 2220
gatgagggaa agggagagga tgaggaagcc cccctgggga tttggtttgg tcttgtgatc 2280
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tgatactgag cccaaagagc attcaatcat tgttttattt gccttctttt cacaccattg 2400
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ttcccagtgg gtgtgggaca tatctggcaa gattttgtgg cactcctggt tacagatact 2820
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<210> 172
<211> 164
<212> PRT
<213> Homo sapiens

<400> 172
Met Trp Asp Leu Val Leu Ser Ile Ala Leu Ser Val Gly Cys Thr Gly
 1   5   10   15
Ala Val Pro Leu Ile Gln Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
            20   25   30
Lys His Ser Gln Pro Trp Gln Val Ala Val Tyr Ser His Gly Trp Ala
        35   40   45
His Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
    50   55   60
His Cys Leu Lys Lys Asn Ser Gln Val Trp Leu Gly Arg His Asn Leu
65   70   75   80
Phe Glu Pro Glu Asp Thr Gly Gln Arg Val Pro Val Ser His Ser Phe
                85   90   95
Pro His Pro Leu Tyr Asn Met Ser Leu Leu Lys His Gln Ser Leu Arg
            100   105   110
Pro Asp Glu Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu
        115   120   125
Pro Ala Lys Ile Thr Asp Val Val Lys Val Leu Gly Leu Pro Thr Gln
    130   135   140
Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile
145   150   155   160
Glu Pro Glu Glu

<210> 173
<211> 1464
<212> DNA
<213> Homo sapiens

<400> 173
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gaggctggga gtgcgagaag cattcccaac cctggcaggt gcttgtggcc tctcgtggca 180
gggcagtctg cggcggtgtt ctggtgcacc cccagtgggt cctcacagct gcccactgca 240
tcaggaacaa aagcgtgatc ttgctgggtc ggcacagcct gtttcatcct gaagacacag 300

gccaggtatt tcaggtcagc cacagcttcc cacacccgct ctacgatatg agcctcctga 360
agaatcgatt cctcaggcca ggtgatgact ccagccacga cctcatgctg ctccgcctgt 420
cagagcctgc cgagctcacg gatgctgtga aggtcatgga cctgcccacc caggagccag 480
cactggggac cacctgctac gcctcaggct ggggcagcat tgaaccagag gagttcttga 540
ccccaaagaa acttcagtgt gtggacctcc atgttatttc caatgacgtg tgtgcgcaag 600
ttcaccctca gaaggtgacc aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa 660
gcacctgctc gggtgattct gggggcccac ttgtctgtaa tggtgtgctt caaggtatca 720
cgtcatgggg cagtgaacca tgtgccctgc ccgaaaggcc ttccctgtac accaaggtgg 780
tgcattaccg gaagtggatc aaggacacca tcgtggccaa cccctgagca cccctatcaa 840
ccccctattg tagtaaactt ggaaccttgg aaatgaccag gccaagactc aagcctcccc 900
agttctactg acctttgtcc ttaggtgtga ggtccagggt tgctaggaaa agaaatcagc 960
agacacaggt gtagaccaga gtgtttctta aatggtgtaa ttttgtcctc tctgtgtcct 1020
ggggaatact ggccatgcct ggagacatat cactcaattt ctctgaggac acagatagga 1080
tggggtgtct gtgttatttg tggggtacag agatgaaaga ggggtgggat ccacactgag 1140
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acaacgcacc agacactcac agcaaggatg gagctgaaaa cataacccac tctgtcctgg 1260
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ggatggggat gaagtaagga gagggactgg acccccctgga agctgattca ctatgggggg 1380
aggtgtattg aagtcctcca gacaaccctc agatttgatg atttcctagt agaactcaca 1440
gaaataaaga gctgttatac tgtg 1464

<210> 174
<211> 261
<212> PRT
<213> Homo sapiens

<400> 174

Met	Trp	Val	Pro	Val	Val	Phe	Leu	Thr	Leu	Ser	Val	Thr	Trp	Ile	Gly
1				5					10					15	
Ala	Ala	Pro	Leu	Ile	Leu	Ser	Arg	Ile	Val	Gly	Gly	Trp	Glu	Cys	Glu
			20					25					30		
Lys	His	Ser	Gln	Pro	Trp	Gln	Val	Leu	Val	Ala	Ser	Arg	Gly	Arg	Ala
		35					40					45			
Val	Cys	Gly	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Thr	Ala	Ala
	50					55					60				
His	Cys	Ile	Arg	Asn	Lys	Ser	Val	Ile	Leu	Leu	Gly	Arg	His	Ser	Leu
65					70					75					80
Phe	His	Pro	Glu	Asp	Thr	Gly	Gln	Val	Phe	Gln	Val	Ser	His	Ser	Phe
				85					90					95	
Pro	His	Pro	Leu	Tyr	Asp	Met	Ser	Leu	Leu	Lys	Asn	Arg	Phe	Leu	Arg
			100					105					110		
Pro	Gly	Asp	Asp	Ser	Ser	His	Asp	Leu	Met	Leu	Leu	Arg	Leu	Ser	Glu
		115					120					125			
Pro	Ala	Glu	Leu	Thr	Asp	Ala	Val	Lys	Val	Met	Asp	Leu	Pro	Thr	Gln
	130					135					140				
Glu	Pro	Ala	Leu	Gly	Thr	Thr	Cys	Tyr	Ala	Ser	Gly	Trp	Gly	Ser	Ile
145					150					155					160
Glu	Pro	Glu	Glu	Phe	Leu	Thr	Pro	Lys	Lys	Leu	Gln	Cys	Val	Asp	Leu
				165					170					175	
His	Val	Ile	Ser	Asn	Asp	Val	Cys	Ala	Gln	Val	His	Pro	Gln	Lys	Val
			180					185					190		
Thr	Lys	Phe	Met	Leu	Cys	Ala	Gly	Arg	Trp	Thr	Gly	Gly	Lys	Ser	Thr
		195					200					205			
Cys	Ser	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Asn	Gly	Val	Leu	Gln
	210					215					220				
Gly	Ile	Thr	Ser	Trp	Gly	Ser	Glu	Pro	Cys	Ala	Leu	Pro	Glu	Arg	Pro
225					230					235					240
Ser	Leu	Tyr	Thr	Lys	Val	Val	His	Tyr	Arg	Lys	Trp	Ile	Lys	Asp	Thr

```
                245                 250                 255
Ile Val Ala Asn Pro
            260
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<210> 175
<211> 1906
<212> DNA
<213> Homo sapiens

<400> 175
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tcctcaccct gtccgtgacg tggattggtg ctgcaccect catcctgtct cggattgtgg 120
gaggctggga gtgcgagaag cattcccaac cctggcaggt gcttgtggcc tctcgtggca 180
gggcagtctg cggcggtgtt ctggtgcacc cccagtgggt cctcacagct gcccactgca 240
tcaggaacaa aagcgtgatc ttgctgggtc ggcacagcct gtttcatcct gaagacacag 300
gccaggtatt tcaggtcagc cacagcttcc cacacccgct ctacgatatg agcctcctga 360
agaatcgatt cctcaggcca ggtgatgact ccagccacga cctcatgctg ctccgcctgt 420
cagagcctgc cgagctcacg gatgctgtga aggtcatgga cctgcccacc caggagccag 480
cactggggac cacctgctac gcctcaggct ggggcagcat tgaaccagag gagttcttga 540
ccccaaagaa acttcagtgt gtggacctcc atgttatttc caatgacgtg tgtgcgcaag 600
ttcaccctca gaaggtgacc aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa 660
gcacctgctc gtgggtcatt ctgatcaccg aactgaccat gccagccctg ccgatggtcc 720
tccatggctc cctagtgccc tggagaggag gtgtctagtc agagagtagt cctggaaggt 780
ggcctctgtg aggagccacg gggacagcat cctgcagatg gtcctggccc ttgtcccacc 840
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agtcccttcc ccaccggcca ggactggagc ccctaccect ctgttggaat ccctgcccac 960
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ccttccctgt acaccaaggt ggtgcattac cggaagtgga tcaaggacac catcgtggcc 1260
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aggccaagac tcaagcctcc ccagttctac tgacctttgt ccttaggtgt gaggtccagg 1380
gttgctagga aaagaaatca gcagacacag gtgtagacca gagtgtttct taaatggtgt 1440
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ttctctgagg acacagatag gatggggtgt ctgtgttatt tgtggggtac agagatgaaa 1560
gaggggtggg atccacactg agagagtgga gagtgacatg tgctggacac tgtccatgaa 1620
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aacataaccc actctgtcct ggaggcactg ggaagcctag agaaggctgt gagccaagga 1740
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gaagctgatt cactatgggg ggaggtgtat tgaagtcctc cagacaaccc tcagatttga 1860
tgatttccta gtagaactca cagaaataaa gagctgttat actgtg 1906

<210> 176
<211> 238
<212> PRT
<213> Homo sapiens

<400> 176
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Met Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly
 1               5                  10                  15
Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
            20                  25                  30
Lys His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala
        35                  40                  45
Val Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
    50                  55                  60
```

```
His Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu
65                  70                  75                  80
Phe His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe
                85                  90                  95
Pro His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg
            100                 105                 110
Pro Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu
        115                 120                 125
Pro Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln
    130                 135                 140
Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile
145                 150                 155                 160
Glu Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu
                165                 170                 175
His Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val
            180                 185                 190
Thr Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Thr
        195                 200                 205
Cys Ser Trp Val Ile Leu Ile Thr Glu Leu Thr Met Pro Ala Leu Pro
    210                 215                 220
Met Val Leu His Gly Ser Leu Val Pro Trp Arg Gly Gly Val
225                 230                 235
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<210> 177
<211> 1335
<212> DNA
<213> Homo sapiens

<400> 177

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gaggctggga gtgcgagaag cattcccaac cctggcaggt gcttgtggcc tctcgtggca 180
gggcagtctg cggcggtgtt ctggtgcacc cccagtgggt cctcacagct gcccactgca 240
tcaggaagcc aggtgatgac tccagccacg acctcatgct gctccgcctg tcagagcctg 300
ccgagctcac ggatgctgtg aaggtcatgg acctgcccac ccaggagcca gcactgggga 360
ccacctgcta cgcctcaggc tggggcagca ttgaaccaga ggagttcttg accccaaaga 420
aacttcagtg tgtggacctc catgttattt ccaatgacgt gtgtgcgcaa gttcaccctc 480
agaaggtgac caagttcatg ctgtgtgctg gacgctggac agggggcaaa agcacctgct 540
cgggtgattc tgggggccca cttgtctgta atggtgtgct tcaaggtatc acgtcatggg 600
gcagtgaacc atgtgccctg cccgaaaggc cttccctgta caccaaggtg gtgcattacc 660
ggaagtggat caaggacacc atcgtggcca acccctgagc acccctatca acccccctatt 720
gtagtaaact tggaaccttg gaaatgacca ggccaagact caagcctccc cagttctact 780
gacctttgtc cttaggtgtg aggtccaggg ttgctaggaa aagaaatcag cagacacagg 840
tgtagaccag agtgtttctt aaatggtgta attttgtcct ctctgtgtcc tggggaatac 900
tggccatgcc tggagacata tcactcaatt tctctgagga cacagatagg atggggtgtc 960
tgtgttattt gtggggtaca gagatgaaag aggggtggga tccacactga gagagtggag 1020
agtgacatgt gctggacact gtccatgaag cactgagcag aagctggagg cacaacgcac 1080
cagacactca cagcaaggat ggagctgaaa acataaccca ctctgtcctg gaggcactgg 1140
gaagcctaga gaaggctgtg agccaaggag ggagggtctt cctttggcat gggatgggga 1200
tgaagtaagg agagggactg gacccccctgg aagctgattc actatggggg gaggtgtatt 1260
gaagtcctcc agacaaccct cagatttgat gatttcctag tagaactcac agaaataaag 1320
agctgttata ctgtg                                                  1335
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<210> 178
<211> 218
<212> PRT
<213> Homo sapiens

<400> 178
Met Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly
1 5 10 15
Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
20 25 30
Lys His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala
35 40 45
Val Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
50 55 60
His Cys Ile Arg Lys Pro Gly Asp Asp Ser Ser His Asp Leu Met Leu
65 70 75 80
Leu Arg Leu Ser Glu Pro Ala Glu Leu Thr Asp Ala Val Lys Val Met
85 90 95
Asp Leu Pro Thr Gln Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser
100 105 110
Gly Trp Gly Ser Ile Glu Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu
115 120 125
Gln Cys Val Asp Leu His Val Ile Ser Asn Asp Val Cys Ala Gln Val
130 135 140
His Pro Gln Lys Val Thr Lys Phe Met Leu Cys Ala Gly Arg Trp Thr
145 150 155 160
Gly Gly Lys Ser Thr Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys
165 170 175
Asn Gly Val Leu Gln Gly Ile Thr Ser Trp Gly Ser Glu Pro Cys Ala
180 185 190
Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val Val His Tyr Arg Lys
195 200 205
Trp Ile Lys Asp Thr Ile Val Ala Asn Pro
210 215

<210> 179
<211> 1341
<212> DNA
<213> Homo sapiens

<400> 179
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tcctcaccct gtccgtgacg tggattggtg ctgcacccct catcctgtct cggattgtgg 120
gaggctggga gtgcgagaag cattcccaac cctggcaggt gcttgtggcc tctcgtggca 180
gggcagtctg cggcggtgtt ctggtgcacc cccagtgggt cctcacagct gcccactgca 240
tcaggaacaa aagcgtgatc ttgctgggtc ggcacagcct gtttcatcct gaagacacag 300
gccaggtatt tcaggtcagc cacagcttcc cacacccgct ctacgatatg agcctcctga 360
agaatcgatt cctcaggcca ggtgatgact ccagcattga accagaggag ttcttgaccc 420
caaagaaact tcagtgtgtg gacctccatg ttatttccaa tgacgtgtgt gcgcaagttc 480
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cctgctcggg tgattctggg ggcccacttg tctgtaatgg tgtgcttcaa ggtatcacgt 600
catggggcag tgaaccatgt gccctgcccg aaaggccttc cctgtacacc aaggtggtgc 660
attaccggaa gtggatcaag gacaccatcg tggccaaccc ctgagcaccc ctatcaaccc 720
cctattgtag taaacttgga accttggaaa tgaccaggcc aagactcaag cctccccagt 780
tctactgacc tttgtcctta ggtgtgaggt ccagggttgc taggaaaaga aatcagcaga 840
cacaggtgta gaccagagtg tttcttaaat ggtgtaattt tgtcctctct gtgtcctggg 900
gaatactggc catgcctgga gacatatcac tcaatttctc tgaggacaca gataggatgg 960
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tggggatgaa gtaaggagag ggactggacc ccctggaagc tgattcacta tgggggggagg 1260
tgtattgaag tcctccagac aaccctcaga tttgatgatt tcctagtaga actcacagaa 1320
ataaagagct gttatactgt g 1341

<210> 180
<211> 220
<212> PRT
<213> Homo sapiens

<400> 180
Met Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly
1 5 10 15
Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
20 25 30
Lys His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala
35 40 45
Val Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
50 55 60
His Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu
65 70 75 80
Phe His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe
85 90 95
Pro His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg
100 105 110
Pro Gly Asp Asp Ser Ser Ile Glu Pro Glu Glu Phe Leu Thr Pro Lys
115 120 125
Lys Leu Gln Cys Val Asp Leu His Val Ile Ser Asn Asp Val Cys Ala
130 135 140
Gln Val His Pro Gln Lys Val Thr Lys Phe Met Leu Cys Ala Gly Arg
145 150 155 160
Trp Thr Gly Gly Lys Ser Thr Cys Ser Gly Asp Ser Gly Gly Pro Leu
165 170 175
Val Cys Asn Gly Val Leu Gln Gly Ile Thr Ser Trp Gly Ser Glu Pro
180 185 190
Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val Val His Tyr
195 200 205
Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro
210 215 220

<210> 181
<211> 555
<212> DNA
<213> Homo sapiens

<400> 181
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tcctcaccct gtccgtgacg tggattggtg ctgcaccccc catcctgtct cggattgtgg 120
gaggctggga gtgcgagaag cattcccaac cctggcaggt gcttgtggcc tctcgtggca 180
gggcagtctg cggcggtgtt ctggtgcacc cccagtgggt cctcacagct gcccactgca 240
tcaggaagtg agtaggggcc tggggtctgg ggagcaggtg tctgtgtccc agaggaataa 300
cagctgggca ttttccccag gataacctct aaggccagcc ttgggactgg gggagagagg 360
gaaagttctg gttcaggtca catggggagg cagggttggg gctggaccac cctccccatg 420
gctgcctggg tctccatctg tgttcctcta tgtctctttg tgtcgctttc attatgtctc 480
ttggtaactg gcttcggttg tgtctctccg tgtgactatt ttgttctctc tctccctctc 540
ttctctgtct tcagt 555

<210> 182

<211> 69
<212> PRT
<213> Homo sapiens

<400> 182
Met Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly
 1   5   10   15
Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu
            20   25   30
Lys His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala
        35   40   45
Val Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala
    50   55   60
His Cys Ile Arg Lys
65

<210> 183
<211> 807
<212> DNA
<213> Homo sapiens

<400> 183
acactctacc accatgaatc cattcctgat ccttgccttt gtgggagctg ctgttgctgt 60
ccccttttgac gatgatgaca agattgttgg gggctacacc tgtgaggaga attctctccc 120
ctaccaggtg tccctgaatt ctggctccca cttctgcggt ggctccctca tcagcgaaca 180
gtgggtggta tcagcagctc actgctacaa gacccgcatc caggtgagac tgggagagca 240
caacatcaaa gtcctggagg ggaatgagca gttcatcaat gcggccaaga tcatccgcca 300
ccctaaatac aacagggaca ctctggacaa tgacatcatg ctgatcaaac tctcctcacc 360
tgccgtcatc aatgcccgcg tgtccaccat ctctctgccc accgcccctc cagctgctgg 420
cactgagtgc ctcatctccg gctggggcaa cactctgagc tttggtgctg actacccaga 480
cgagctgaag tgcctggatg ctccggtgct gacccaggct gagtgtaaag cctcctaccc 540
tggaaagatt accaacagca tgttctgtgt gggcttcctt gagggaggca aggattcctg 600
ccagcgtgac tctggtggcc ctgtggtctg caacggacag ctccaaggag ttgtctcctg 660
gggccatggc tgtgcctgga agaacaggcc tggagtctac accaaggtct acaactatgt 720
ggactggatt aaggacacca tcgctgccaa cagctaaagc ccccggtccc tctgcagtct 780
ctataccaat aaagtggccc tgctctc 807

<210> 184
<211> 247
<212> PRT
<213> Homo sapiens

<400> 184
Met Asn Pro Phe Leu Ile Leu Ala Phe Val Gly Ala Ala Val Ala Val
 1   5   10   15
Pro Phe Asp Asp Asp Asp Lys Ile Val Gly Gly Tyr Thr Cys Glu Glu
            20   25   30
Asn Ser Leu Pro Tyr Gln Val Ser Leu Asn Ser Gly Ser His Phe Cys
        35   40   45
Gly Gly Ser Leu Ile Ser Glu Gln Trp Val Val Ser Ala Ala His Cys
    50   55   60
Tyr Lys Thr Arg Ile Gln Val Arg Leu Gly Glu His Asn Ile Lys Val
65   70   75   80
Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile Ile Arg His
                85   90   95
Pro Lys Tyr Asn Arg Asp Thr Leu Asp Asn Asp Ile Met Leu Ile Lys
            100   105   110

```
Leu Ser Ser Pro Ala Val Ile Asn Ala Arg Val Ser Thr Ile Ser Leu
        115                 120                 125
Pro Thr Ala Pro Pro Ala Ala Gly Thr Glu Cys Leu Ile Ser Gly Trp
    130                 135                 140
Gly Asn Thr Leu Ser Phe Gly Ala Asp Tyr Pro Asp Glu Leu Lys Cys
145                 150                 155                 160
Leu Asp Ala Pro Val Leu Thr Gln Ala Glu Cys Lys Ala Ser Tyr Pro
                165                 170                 175
Gly Lys Ile Thr Asn Ser Met Phe Cys Val Gly Phe Leu Glu Gly Gly
            180                 185                 190
Lys Asp Ser Cys Gln Arg Asp Ser Gly Gly Pro Val Val Cys Asn Gly
        195                 200                 205
Gln Leu Gln Gly Val Val Ser Trp Gly His Gly Cys Ala Trp Lys Asn
    210                 215                 220
Arg Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Asp Trp Ile Lys
225                 230                 235                 240
Asp Thr Ile Ala Ala Asn Ser
                245
```

<210> 185
<211> 1055
<212> DNA
<213> Homo sapiens

<400> 185
acctgcattt ccaccacctg ttctgggagt ggggcccagt cagccccctt tgcttacctt 60
ctgccctata ttagagcccc aggttctgtg ccctttttct atcatcgcaa aactcatgat 120
gctccggctg ctcagttccc tcctccttgt ggccgttgcc tcaggctatg gcccaccttc 180
ctctcgccct tccagccgcg ttgtcaatgg tgaggatgcg gtcccctaca gctggccctg 240
gcaggtttcc ctgcagtatg agaaaagcgg aagcttctac cacacctgtg gcggtagcct 300
catcgccccc gactgggttg tgactgccgg ccactgcatc tcgagctccc ggacctacca 360
ggtggtgttg ggcgagtacg accgtgctgt gaaggagggc cccgagcagg tgatccccat 420
caactctggg gacctctttg tgcatccact ctggaaccgc tcgtgtgtgg cctgtggcaa 480
tgacatcgcc ctcatcaagc tctcacgcag cgcccagctg ggagacgccg tccagctcgc 540
ctcactccct ccggctggtg acatccttcc caacgagaca ccctgctaca tcaccggctg 600
gggccgtctc tataccaacg ggccactccc agacaagctg caggaggccc tgctgccggt 660
ggtggactat gaacactgct ccaggtggaa ctggtggggt tcctccgtga agaagaccat 720
ggtgtgtgct ggaggggaca tccgctccgg ctgcaatggt gactctggag gacccctcaa 780
ctgccccaca gaggatggtg gctggcaggt ccatggcgtg accagctttg tttctgcctt 840
tggctgcaac acccgcagga agcccacggt gttcactcga gtctccgcct tcattgactg 900
gattgaggag accatagcaa gccactagaa ccaaggccca gctggcagtg ctgatcgatc 960
ccacatcctg aataaagaat aaagatctct cagaaaattc caaaaaaaaa aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa   1055

<210> 186
<211> 270
<212> PRT
<213> Homo sapiens

<400> 186
```
Met Met Leu Arg Leu Leu Ser Ser Leu Leu Leu Val Ala Val Ala Ser
 1               5                  10                  15
Gly Tyr Gly Pro Pro Ser Ser Arg Pro Ser Ser Arg Val Val Asn Gly
            20                  25                  30
Glu Asp Ala Val Pro Tyr Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
        35                  40                  45
Glu Lys Ser Gly Ser Phe Tyr His Thr Cys Gly Gly Ser Leu Ile Ala
```

```
    50                  55                  60
Pro Asp Trp Val Val Thr Ala Gly His Cys Ile Ser Ser Ser Arg Thr
65                  70                  75                  80
Tyr Gln Val Val Leu Gly Glu Tyr Asp Arg Ala Val Lys Glu Gly Pro
                85                  90                  95
Glu Gln Val Ile Pro Ile Asn Ser Gly Asp Leu Phe Val His Pro Leu
            100                 105                 110
Trp Asn Arg Ser Cys Val Ala Cys Gly Asn Asp Ile Ala Leu Ile Lys
        115                 120                 125
Leu Ser Arg Ser Ala Gln Leu Gly Asp Ala Val Gln Leu Ala Ser Leu
    130                 135                 140
Pro Pro Ala Gly Asp Ile Leu Pro Asn Glu Thr Pro Cys Tyr Ile Thr
145                 150                 155                 160
Gly Trp Gly Arg Leu Tyr Thr Asn Gly Pro Leu Pro Asp Lys Leu Gln
                165                 170                 175
Glu Ala Leu Leu Pro Val Val Asp Tyr Glu His Cys Ser Arg Trp Asn
            180                 185                 190
Trp Trp Gly Ser Ser Val Lys Lys Thr Met Val Cys Ala Gly Gly Asp
        195                 200                 205
Ile Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Pro
    210                 215                 220
Thr Glu Asp Gly Gly Trp Gln Val His Gly Val Thr Ser Phe Val Ser
225                 230                 235                 240
Ala Phe Gly Cys Asn Thr Arg Arg Lys Pro Thr Val Phe Thr Arg Val
                245                 250                 255
Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser His
            260                 265                 270
```

<210> 187
<211> 941
<212> DNA
<213> Homo sapiens

<400> 187

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cttacagaac tcccacggac acaccatgat taggaccctg ctgctgtcca ctttggtggc 60
tggagccctc agttgtgggg tctccactta cgcgcctgat atgtctagga tgcttggagg 120
tgaagaagcg aggcccaaca gctggccctg gcaggtctcc ctgcagtaca gctccaatgg 180
ccagtggtac cacacctgcg gagggtccct gatagccaac agctgggtcc tgacggctgc 240
ccactgcatc agctcctccg ggatctaccg cgtgatgctg ggccagcata acctctacgt 300
tgcagagtcc ggctcgctgg ccgtcagtgt ctctaagatt gtggtgcaca aggactggaa 360
ctccgaccag gtctccaaag ggaacgacat tgccctgctc aaactggcta accccgtctc 420
cctcaccgac aagatccagc tggcctgcct ccctcctgcc ggcaccattc tacccaacaa 480
ctacccctgc tacgtcacgg gctggggaag gctgcagacc aacggggctc tccctgatga 540
cctgaagcag ggccggttgc tggttgtgga ctatgccacc tgctccagct ctggctggtg 600
gggcagcacc gtgaagacga atatgatctg tgctgggggt gatggcgtga tatgcacctg 660
caacggagac tccggtgggc cgctgaactg tcaggcatct gacggccggt gggaggtgca 720
tggcatcggc agcctcacgt cggtccttgg ttgcaactac tactacaagc cctccatctt 780
cacgcgggtc tccaactaca acgactggat caattcggtg attgcaaata actaaccaaa 840
agaagtccct gggactgttt cagacttgga aaggtcacag aaggaaaata atattatata 900
aagtgacaac tatgcaaatc acaaaaaaaa aaaaaaaaaa a                     941
```

<210> 188
<211> 269
<212> PRT
<213> Homo sapiens

<400> 188

```
Met Ile Arg Thr Leu Leu Leu Ser Thr Leu Val Ala Gly Ala Leu Ser
 1               5                  10                  15
Cys Gly Val Ser Thr Tyr Ala Pro Asp Met Ser Arg Met Leu Gly Gly
            20                  25                  30
Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
        35                  40                  45
Ser Ser Asn Gly Gln Trp Tyr His Thr Cys Gly Gly Ser Leu Ile Ala
    50                  55                  60
Asn Ser Trp Val Leu Thr Ala Ala His Cys Ile Ser Ser Ser Gly Ile
65                  70                  75                  80
Tyr Arg Val Met Leu Gly Gln His Asn Leu Tyr Val Ala Glu Ser Gly
                85                  90                  95
Ser Leu Ala Val Ser Val Ser Lys Ile Val Val His Lys Asp Trp Asn
            100                 105                 110
Ser Asp Gln Val Ser Lys Gly Asn Asp Ile Ala Leu Leu Lys Leu Ala
        115                 120                 125
Asn Pro Val Ser Leu Thr Asp Lys Ile Gln Leu Ala Cys Leu Pro Pro
    130                 135                 140
Ala Gly Thr Ile Leu Pro Asn Asn Tyr Pro Cys Tyr Val Thr Gly Trp
145                 150                 155                 160
Gly Arg Leu Gln Thr Asn Gly Ala Leu Pro Asp Asp Leu Lys Gln Gly
                165                 170                 175
Arg Leu Leu Val Val Asp Tyr Ala Thr Cys Ser Ser Ser Gly Trp Trp
            180                 185                 190
Gly Ser Thr Val Lys Thr Asn Met Ile Cys Ala Gly Gly Asp Gly Val
        195                 200                 205
Ile Cys Thr Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Gln Ala
    210                 215                 220
Ser Asp Gly Arg Trp Glu Val His Gly Ile Gly Ser Leu Thr Ser Val
225                 230                 235                 240
Leu Gly Cys Asn Tyr Tyr Tyr Lys Pro Ser Ile Phe Thr Arg Val Ser
                245                 250                 255
Asn Tyr Asn Asp Trp Ile Asn Ser Val Ile Ala Asn Asn
            260                 265
```

<210> 189
<211> 2048
<212> DNA
<213> Homo sapiens

<400> 189

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ctattgatct ggactcctgg ataggcagct ggaccaacgg acggacgcca tgagggctct 60
gctgctcctg gggttcctgc tggtgagctt ggagtcaaca ctttcgattc caccttggga 120
agcccccaag gagcataagt acaaagctga agagcacaca gtcgttctca ctgtcaccgg 180
ggagccctgc cacttccgct tccagtacca ccggcagctg taccacaaat gtacccacaa 240
gggccggcca ggccctcagc cctggtgtgc taccaccccc aactttgatc aggaccagcg 300
atggggatac tgtttggagc ccaagaaagt gaaagaccac tgcagcaaac acagcccctg 360
ccagaaagga gggacctgtg tgaacatgcc aagcggcccc cactgtctct gtccacaaca 420
cctcactgga aaccactgcc agaaagagaa gtgctttgag cctcagcttc tccggttttt 480
ccacaagaat gagatatggt atagaactga gcaagcagct gtggccagat gccagtgcaa 540
gggtcctgat gcccactgcc agcggctggc cagccaggcc tgccgcacca acccgtgcct 600
ccatgggggt cgctgcctag aggtggaggg ccaccgcctg tgccactgcc cggtgggcta 660
caccggaccc ttctgcgacg tggacaccaa ggcaagctgc tatgatggcc gcgggctcag 720
ctaccgcggc ctggccagga ccacgctctc gggtgcgccc tgtcagccgt gggcctcgga 780
ggccacctac cggaacgtga ctgccgagca agcgcggaac tggggactgg gcggccacgc 840
cttctgccgg aacccggaca acgacatccg cccgtggtgc ttcgtgctga accgcgaccg 900
gctgagctgg gagtactgcg acctggcaca gtgccagacc ccaacccagg cggcgcctcc 960
```

```
gaccccggtg tcccctaggc ttcatgtccc actcatgccc gcgcagccgg caccgccgaa 1020
gcctcagccc acgacccgga ccccgcctca gtcccagacc ccgggagcct tgccggcgaa 1080
gcgggagcag ccgccttccc tgaccaggaa cggcccactg agctgcgggc agcggctccg 1140
caagagtctg tcttcgatga cccgcgtcgt tggcgggctg gtggcgctac gcggggcgca 1200
cccctacatc gccgcgctgt actggggcca cagtttctgc gccggcagcc tcatcgcccc 1260
ctgctgggtg ctgacggccg ctcactgcct gcaggaccgg cccgcacccg aggatctgac 1320
ggtggtgctc ggccaggaac gccgtaacca cagctgtgag ccgtgccaga cgttggccgt 1380
gcgctcctac cgcttgcacg aggccttctc gcccgtcagc taccagcacg acctggctct 1440
gttgcgcctt caggaggatg cggacggcag ctgcgcgctc ctgtcgcctt acgttcagcc 1500
ggtgtgcctg ccaagcggcg ccgcgcgacc ctccgagacc acgctctgcc aggtggccgg 1560
ctggggccac cagttcgagg gggcggagga atatgccagc ttcctgcagg aggcgcaggt 1620
accgttcctc tccctggagc gctgctcagc cccggacgtg cacggatcct ccatcctccc 1680
cggcatgctc tgcgcagggt tcctcgaggg cggcaccgat gcgtgccagg gtgattccgg 1740
aggcccgctg gtgtgtgagg accaagctgc agagcgccgg ctcaccctgc aaggcatcat 1800
cagctgggga tcgggctgtg gtgaccgcaa caagccaggc gtctacaccg atgtggccta 1860
ctacctggcc tggatccggg agcacaccgt ttcctgattg ctcagggact catctttccc 1920
tccttggtga ttccgcagtg agagagtggc tggggcatgg aaggcaagat tgtgtcccat 1980
tcccccagtg cggccagctc cgcgccagga tggcgaggaa ctcaataaag tgctttgaaa 2040
atgctgag                                                          2048
```

<210> 190
<211> 615
<212> PRT
<213> Homo sapiens

<400> 190

```
Met Arg Ala Leu Leu Leu Leu Gly Phe Leu Leu Val Ser Leu Glu Ser
 1               5                  10                  15
Thr Leu Ser Ile Pro Pro Trp Glu Ala Pro Lys Glu His Lys Tyr Lys
            20                  25                  30
Ala Glu Glu His Thr Val Val Leu Thr Val Thr Gly Glu Pro Cys His
        35                  40                  45
Phe Pro Phe Gln Tyr His Arg Gln Leu Tyr His Lys Cys Thr His Lys
    50                  55                  60
Gly Arg Pro Gly Pro Gln Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp
65                  70                  75                  80
Gln Asp Gln Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp
                85                  90                  95
His Cys Ser Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn
            100                 105                 110
Met Pro Ser Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn
        115                 120                 125
His Cys Gln Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Arg Phe Phe
    130                 135                 140
His Lys Asn Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg
145                 150                 155                 160
Cys Gln Cys Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln
                165                 170                 175
Ala Cys Arg Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val
            180                 185                 190
Glu Gly His Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Pro Phe
        195                 200                 205
Cys Asp Val Asp Thr Lys Ala Ser Cys Tyr Asp Gly Arg Gly Leu Ser
    210                 215                 220
Tyr Arg Gly Leu Ala Arg Thr Thr Leu Ser Gly Ala Pro Cys Gln Pro
225                 230                 235                 240
Trp Ala Ser Glu Ala Thr Tyr Arg Asn Val Thr Ala Glu Gln Ala Arg
                245                 250                 255
```

```
Asn Trp Gly Leu Gly Gly His Ala Phe Cys Arg Asn Pro Asp Asn Asp
            260                 265                 270
Ile Arg Pro Trp Cys Phe Val Leu Asn Arg Asp Arg Leu Ser Trp Glu
        275                 280                 285
Tyr Cys Asp Leu Ala Gln Cys Gln Thr Pro Thr Gln Ala Ala Pro Pro
    290                 295                 300
Thr Pro Val Ser Pro Arg Leu His Val Pro Leu Met Pro Ala Gln Pro
305                 310                 315                 320
Ala Pro Pro Lys Pro Gln Pro Thr Thr Arg Thr Pro Pro Gln Ser Gln
                325                 330                 335
Thr Pro Gly Ala Leu Pro Ala Lys Arg Glu Gln Pro Pro Ser Leu Thr
            340                 345                 350
Arg Asn Gly Pro Leu Ser Cys Gly Gln Arg Leu Arg Lys Ser Leu Ser
        355                 360                 365
Ser Met Thr Arg Val Val Gly Gly Leu Val Ala Leu Arg Gly Ala His
    370                 375                 380
Pro Tyr Ile Ala Ala Leu Tyr Trp Gly His Ser Phe Cys Ala Gly Ser
385                 390                 395                 400
Leu Ile Ala Pro Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asp
                405                 410                 415
Arg Pro Ala Pro Glu Asp Leu Thr Val Val Leu Gly Gln Glu Arg Arg
            420                 425                 430
Asn His Ser Cys Glu Pro Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg
        435                 440                 445
Leu His Glu Ala Phe Ser Pro Val Ser Tyr Gln His Asp Leu Ala Leu
    450                 455                 460
Leu Arg Leu Gln Glu Asp Ala Asp Gly Ser Cys Ala Leu Leu Ser Pro
465                 470                 475                 480
Tyr Val Gln Pro Val Cys Leu Pro Ser Gly Ala Ala Arg Pro Ser Glu
                485                 490                 495
Thr Thr Leu Cys Gln Val Ala Gly Trp Gly His Gln Phe Glu Gly Ala
            500                 505                 510
Glu Glu Tyr Ala Ser Phe Leu Gln Glu Ala Gln Val Pro Phe Leu Ser
        515                 520                 525
Leu Glu Arg Cys Ser Ala Pro Asp Val His Gly Ser Ser Ile Leu Pro
    530                 535                 540
Gly Met Leu Cys Ala Gly Phe Leu Glu Gly Gly Thr Asp Ala Cys Gln
545                 550                 555                 560
Gly Asp Ser Gly Gly Pro Leu Val Cys Glu Asp Gln Ala Ala Glu Arg
                565                 570                 575
Arg Leu Thr Leu Gln Gly Ile Ile Ser Trp Gly Ser Gly Cys Gly Asp
            580                 585                 590
Arg Asn Lys Pro Gly Val Tyr Thr Asp Val Ala Tyr Tyr Leu Ala Trp
        595                 600                 605
Ile Arg Glu His Thr Val Ser
    610                 615
```

<210> 191
<211> 2245
<212> DNA
<213> Homo sapiens

<400> 191
agaacagctt gaagaccgtt catttttaag tgacaagaga ctcacctcca agaagcaatt 60
gtgttttcag aatgatttta ttcaagcaag caacttattt catttccttg tttgctacag 120
tttcctgtgg atgtctgact caactctatg aaaacgcctt cttcagaggt ggggatgtag 180
cttccatgta caccccaaat gcccaatact gccagatgag gtgcacattc cacccaaggt 240

gtttgctatt cagttttctt ccagcaagtt caatcaatga catggagaaa aggtttggtt 300
gcttcttgaa agatagtgtt acaggaaccc tgccaaaagt acatcgaaca ggtgcagttt 360
ctggacattc cttgaagcaa tgtggtcatc aaataagtgc ttgccatcga gacatttata 420
aaggagttga tatgagagga gtcaatttta atgtgtctaa ggttagcagt gttgaagaat 480
gccaaaaaag gtgcaccaat aacattcgct gccagttttt ttcatatgcc acgcaaacat 540
ttcacaaggc agagtaccgg aacaattgcc tattaaagta cagtcccgga ggaacaccta 600
ccgctataaa ggtgctgagt aacgtggaat ctggattctc actgaagccc tgtgcccttt 660
cagaaattgg ttgccacatg aacatcttcc agcatcttgc gttctcagat gtggatgttg 720
ccagggttct cactccagat gcttttgtgt gtcggaccat ctgcacctat caccccaact 780
gcctcttctt tacattctat acaaatgtat ggaaaatcga gtcacaaaga aatgtttgtc 840
ttcttaaaac atctgaaagt ggcacaccaa gttcctctac tcctcaagaa aacaccatat 900
ctggatatag ccttttaacc tgcaaaagaa ctttacctga accctgccat tctaaaattt 960
acccgggagt tgactttgga ggagaagaat tgaatgtgac ttttgttaaa ggagtgaatg 1020
tttgccaaga gacttgcaca aagatgattc gctgtcagtt tttcacttat tctttactcc 1080
cagaagactg taaggaagag aagtgtaagt gtttcttaag attatctatg gatggttctc 1140
caactaggat tgcgtatggg acacaaggga gctctggtta ctctttgaga ttgtgtaaca 1200
ctggggacaa ctctgtctgc acaacaaaaa caagcacacg cattgttgga ggaacaaact 1260
cttcttgggg agagtggccc tggcaggtga gcctgcaggt gaagctgaca gctcagaggc 1320
acctgtgtgg agggtcactc ataggacacc agtgggtcct cactgctgcc cactgctttg 1380
atgggcttcc cctgcaggat gtttggcgca tctatagtgg cattttaaat ctgtcagaca 1440
ttacaaaaga tacacctttc tcacaaataa aagagattat tattcaccaa aactataaag 1500
tctcagaagg gaatcatgat atcgccttga taaaactcca ggctcctttg aattacactg 1560
aattccaaaa accaatatgc ctaccttcca aaggtgacac aagcacaatt tataccaact 1620
gttgggtaac cggatggggc ttctcgaagg agaaaggtga aatccaaaat attctacaaa 1680
aggtaaatat tcctttggta acaaatgaag aatgccagaa aagatatcaa gattataaaa 1740
taacccaacg gatggtctgt gctggctata aagaaggggg aaaagatgct tgtaagggag 1800
attcaggtgg tcccttagtt tgcaaacaca acggaatgtg gcgtttggtg ggcatcacaa 1860
gctggggtga aggctgtgcc cgcagggagc aacctggtgt ctacaccaaa gtcgctgagt 1920
acatggactg gattttagag aaaacacaga gcagtgatgg aaaagctcag atgcagtcac 1980
cagcatgaga agcagtccag agtctaggca atttttacaa cctgagttca agtcaaattc 2040
tgagcctggg gggtcctcat ctgcaaagca tggagagtgg catcttcttt gcatcctaag 2100
gacgaaagac acagtgcact cagagctgct gaggacaatg tctgctgaag cccgctttca 2160
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ttgtgaaata aaatggtgaa agatc 2245

<210> 192
<211> 638
<212> PRT
<213> Homo sapiens

<400> 192

Met	Ile	Leu	Phe	Lys	Gln	Ala	Thr	Tyr	Phe	Ile	Ser	Leu	Phe	Ala	Thr
1				5				10					15		
Val	Ser	Cys	Gly	Cys	Leu	Thr	Gln	Leu	Tyr	Glu	Asn	Ala	Phe	Phe	Arg
			20					25				30			
Gly	Gly	Asp	Val	Ala	Ser	Met	Tyr	Thr	Pro	Asn	Ala	Gln	Tyr	Cys	Gln
		35					40					45			
Met	Arg	Cys	Thr	Phe	His	Pro	Arg	Cys	Leu	Leu	Phe	Ser	Phe	Leu	Pro
	50					55					60				
Ala	Ser	Ser	Ile	Asn	Asp	Met	Glu	Lys	Arg	Phe	Gly	Cys	Phe	Leu	Lys
65					70					75					80
Asp	Ser	Val	Thr	Gly	Thr	Leu	Pro	Lys	Val	His	Arg	Thr	Gly	Ala	Val
				85					90					95	
Ser	Gly	His	Ser	Leu	Lys	Gln	Cys	Gly	His	Gln	Ile	Ser	Ala	Cys	His
			100					105					110		
Arg	Asp	Ile	Tyr	Lys	Gly	Val	Asp	Met	Arg	Gly	Val	Asn	Phe	Asn	Val
		115					120					125			
Ser	Lys	Val	Ser	Ser	Val	Glu	Glu	Cys	Gln	Lys	Arg	Cys	Thr	Asn	Asn

```
    130                 135                 140
Ile Arg Cys Gln Phe Phe Ser Tyr Ala Thr Gln Thr Phe His Lys Ala
145                 150                 155                 160
Glu Tyr Arg Asn Asn Cys Leu Leu Lys Tyr Ser Pro Gly Gly Thr Pro
                165                 170                 175
Thr Ala Ile Lys Val Leu Ser Asn Val Glu Ser Gly Phe Ser Leu Lys
            180                 185                 190
Pro Cys Ala Leu Ser Glu Ile Gly Cys His Met Asn Ile Phe Gln His
        195                 200                 205
Leu Ala Phe Ser Asp Val Asp Val Ala Arg Val Leu Thr Pro Asp Ala
    210                 215                 220
Phe Val Cys Arg Thr Ile Cys Thr Tyr His Pro Asn Cys Leu Phe Phe
225                 230                 235                 240
Thr Phe Tyr Thr Asn Val Trp Lys Ile Glu Ser Gln Arg Asn Val Cys
                245                 250                 255
Leu Leu Lys Thr Ser Glu Ser Gly Thr Pro Ser Ser Ser Thr Pro Gln
            260                 265                 270
Glu Asn Thr Ile Ser Gly Tyr Ser Leu Leu Thr Cys Lys Arg Thr Leu
        275                 280                 285
Pro Glu Pro Cys His Ser Lys Ile Tyr Pro Gly Val Asp Phe Gly Gly
    290                 295                 300
Glu Glu Leu Asn Val Thr Phe Val Lys Gly Val Asn Val Cys Gln Glu
305                 310                 315                 320
Thr Cys Thr Lys Met Ile Arg Cys Gln Phe Phe Thr Tyr Ser Leu Leu
                325                 330                 335
Pro Glu Asp Cys Lys Glu Glu Lys Cys Lys Cys Phe Leu Arg Leu Ser
            340                 345                 350
Met Asp Gly Ser Pro Thr Arg Ile Ala Tyr Gly Thr Gln Gly Ser Ser
        355                 360                 365
Gly Tyr Ser Leu Arg Leu Cys Asn Thr Gly Asp Asn Ser Val Cys Thr
    370                 375                 380
Thr Lys Thr Ser Thr Arg Ile Val Gly Gly Thr Asn Ser Ser Trp Gly
385                 390                 395                 400
Glu Trp Pro Trp Gln Val Ser Leu Gln Val Lys Leu Thr Ala Gln Arg
                405                 410                 415
His Leu Cys Gly Gly Ser Leu Ile Gly His Gln Trp Val Leu Thr Ala
            420                 425                 430
Ala His Cys Phe Asp Gly Leu Pro Leu Gln Asp Val Trp Arg Ile Tyr
        435                 440                 445
Ser Gly Ile Leu Asn Leu Ser Asp Ile Thr Lys Asp Thr Pro Phe Ser
    450                 455                 460
Gln Ile Lys Glu Ile Ile Ile His Gln Asn Tyr Lys Val Ser Glu Gly
465                 470                 475                 480
Asn His Asp Ile Ala Leu Ile Lys Leu Gln Ala Pro Leu Asn Tyr Thr
                485                 490                 495
Glu Phe Gln Lys Pro Ile Cys Leu Pro Ser Lys Gly Asp Thr Ser Thr
            500                 505                 510
Ile Tyr Thr Asn Cys Trp Val Thr Gly Trp Gly Phe Ser Lys Glu Lys
        515                 520                 525
Gly Glu Ile Gln Asn Ile Leu Gln Lys Val Asn Ile Pro Leu Val Thr
    530                 535                 540
Asn Glu Glu Cys Gln Lys Arg Tyr Gln Asp Tyr Lys Ile Thr Gln Arg
545                 550                 555                 560
Met Val Cys Ala Gly Tyr Lys Glu Gly Gly Lys Asp Ala Cys Lys Gly
                565                 570                 575
Asp Ser Gly Gly Pro Leu Val Cys Lys His Asn Gly Met Trp Arg Leu
            580                 585                 590
Val Gly Ile Thr Ser Trp Gly Glu Gly Cys Ala Arg Arg Glu Gln Pro
```

595 600 605
Gly Val Tyr Thr Lys Val Ala Glu Tyr Met Asp Trp Ile Leu Glu Lys
610 615 620
Thr Gln Ser Ser Asp Gly Lys Ala Gln Met Gln Ser Pro Ala
625 630 635

<210> 193
<211> 2217
<212> DNA
<213> Homo sapiens

<400> 193
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aaaagcaccc ttattaagaa ttgcagcaag taagccaaca aggtcttttc aggatgattt 180
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ccaagtactg ccaggtagtc tgcacttacc acccaagatg tttactcttc actttcacgg 360
cggaatcacc atctgaggat cccacccgat ggtttacttg tgtcctgaaa gacagtgtta 420
cagaaacact gccaagagtg aataggacag cagcgatttc tgggtattct ttcaagcaat 480
gctcacacca aataagcgct tgcaacaaag acatttatgt ggacctagac atgaagggca 540
taaactataa cagctcagtt gccaagagtg ctcaagaatg ccaagaaaga tgcacggatg 600
acgtccactg ccacttttтc acgtacgcca caaggcagtt tcccagcctg gagcatcgta 660
acatttgtct actgaagcac acccaaacag ggacaccaac cagaataacg aagctcgata 720
aagtggtgtc tggattttca ctgaaatcct gtgcactttc taatctggct tgtattaggg 780
acattttccc taatacggtg tttgcagaca gcaacatcga cagtgtcatg gctcccgatg 840
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ggagagggtg ttgagttcac tgtgccagca tgcttcctcc acagtaacac gctgaagggg 2160
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<210> 194
<211> 625
<212> PRT
<213> Homo sapiens

<400> 194
Met Ile Phe Leu Tyr Gln Val Val His Phe Ile Leu Phe Thr Ser Val

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            20                  25                  30
Gly Asp Ile Thr Thr Val Phe Thr Pro Ser Ala Lys Tyr Cys Gln Val
        35                  40                  45
Val Cys Thr Tyr His Pro Arg Cys Leu Leu Phe Thr Phe Thr Ala Glu
    50                  55                  60
Ser Pro Ser Glu Asp Pro Thr Arg Trp Phe Thr Cys Val Leu Lys Asp
65                  70                  75                  80
Ser Val Thr Glu Thr Leu Pro Arg Val Asn Arg Thr Ala Ala Ile Ser
                85                  90                  95
Gly Tyr Ser Phe Lys Gln Cys Ser His Gln Ile Ser Ala Cys Asn Lys
            100                 105                 110
Asp Ile Tyr Val Asp Leu Asp Met Lys Gly Ile Asn Tyr Asn Ser Ser
        115                 120                 125
Val Ala Lys Ser Ala Gln Glu Cys Gln Glu Arg Cys Thr Asp Asp Val
    130                 135                 140
His Cys His Phe Phe Thr Tyr Ala Thr Arg Gln Phe Pro Ser Leu Glu
145                 150                 155                 160
His Arg Asn Ile Cys Leu Leu Lys His Thr Gln Thr Gly Thr Pro Thr
                165                 170                 175
Arg Ile Thr Lys Leu Asp Lys Val Val Ser Gly Phe Ser Leu Lys Ser
            180                 185                 190
Cys Ala Leu Ser Asn Leu Ala Cys Ile Arg Asp Ile Phe Pro Asn Thr
        195                 200                 205
Val Phe Ala Asp Ser Asn Ile Asp Ser Val Met Ala Pro Asp Ala Phe
    210                 215                 220
Val Cys Gly Arg Ile Cys Thr His His Pro Gly Cys Leu Phe Phe Thr
225                 230                 235                 240
Phe Phe Ser Gln Glu Trp Pro Lys Glu Ser Gln Arg Asn Leu Cys Leu
                245                 250                 255
Leu Lys Thr Ser Glu Ser Gly Leu Pro Ser Thr Arg Ile Lys Lys Ser
            260                 265                 270
Lys Ala Leu Ser Gly Phe Ser Leu Gln Ser Cys Arg His Ser Ile Pro
        275                 280                 285
Val Phe Cys His Ser Ser Phe Tyr His Asp Thr Asp Phe Leu Gly Glu
    290                 295                 300
Glu Leu Asp Ile Val Ala Ala Lys Ser His Glu Ala Cys Gln Lys Leu
305                 310                 315                 320
Cys Thr Asn Ala Val Arg Cys Gln Phe Phe Thr Tyr Thr Pro Ala Gln
                325                 330                 335
Ala Ser Cys Asn Glu Gly Lys Gly Lys Cys Tyr Leu Lys Leu Ser Ser
            340                 345                 350
Asn Gly Ser Pro Thr Lys Ile Leu His Gly Arg Gly Gly Ile Ser Gly
        355                 360                 365
Tyr Thr Leu Arg Leu Cys Lys Met Asp Asn Glu Cys Thr Thr Lys Ile
    370                 375                 380
Lys Pro Arg Ile Val Gly Gly Thr Ala Ser Val Arg Gly Glu Trp Pro
385                 390                 395                 400
Trp Gln Val Thr Leu His Thr Thr Ser Pro Thr Gln Arg His Leu Cys
                405                 410                 415
Gly Gly Ser Ile Ile Gly Asn Gln Trp Ile Leu Thr Ala Ala His Cys
            420                 425                 430
Phe Tyr Gly Val Glu Ser Pro Lys Ile Leu Arg Val Tyr Ser Gly Ile
        435                 440                 445
Leu Asn Gln Ser Glu Ile Lys Glu Asp Thr Ser Phe Phe Gly Val Gln
    450                 455                 460
Glu Ile Ile Ile His Asp Gln Tyr Lys Met Ala Glu Ser Gly Tyr Asp
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465                 470                 475                 480
Ile Ala Leu Leu Lys Leu Glu Thr Thr Val Asn Tyr Thr Asp Ser Gln
                485                 490                 495
Arg Pro Ile Cys Leu Pro Ser Lys Gly Asp Arg Asn Val Ile Tyr Thr
            500                 505                 510
Asp Cys Trp Val Thr Gly Trp Gly Tyr Arg Lys Leu Arg Asp Lys Ile
        515                 520                 525
Gln Asn Thr Leu Gln Lys Ala Lys Ile Pro Leu Val Thr Asn Glu Glu
    530                 535                 540
Cys Gln Lys Arg Tyr Arg Gly His Lys Ile Thr His Lys Met Ile Cys
545                 550                 555                 560
Ala Gly Tyr Arg Glu Gly Gly Lys Asp Ala Cys Lys Gly Asp Ser Gly
                565                 570                 575
Gly Pro Leu Ser Cys Lys His Asn Glu Val Trp His Leu Val Gly Ile
            580                 585                 590
Thr Ser Trp Gly Glu Gly Cys Ala Gln Arg Glu Arg Pro Gly Val Tyr
        595                 600                 605
Thr Asn Val Val Glu Tyr Val Asp Trp Ile Leu Glu Lys Thr Gln Ala
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Val
625
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<210> 195
<211> 2055
<212> DNA
<213> Homo sapiens

<400> 195

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tcttatatca agtggtacat ttcattttat ttacttcagt ttctggtgaa tgtgtgactc 240
agttgttgaa ggacacctgc tttgaaggag gggacattac tacggtcttc acaccaagcg 300
ccaagtactg ccaggtagtc tgcacttacc acccaagatg tttactcttc actttcacgg 360
cggaatcacc atctgaggat cccacccgat ggtttacttg tgtcctgaaa gacagtgtta 420
cagaaacact gccaagagtg aataggacag cagcgatttc tgggtattct ttcaagcaat 480
gctcacacca aataagtaac atttgtctac tgaagcacac ccaaacaggg acaccaacca 540
gaataacgaa gctcgataaa gtggtgtctg gattttcact gaaatcctgt gcactttcta 600
atctggcttg tattagggac attttcccta atacggtgtt tgcagacagc aacatcgaca 660
gtgtcatggc tcccgatgct tttgtctgtg gccgaatctg cactcatcat cccggttgct 720
tgttttttac cttcttttcc caggaatggc ccaaagaatc tcaaagaaat ctttgtctcc 780
ttaaaacatc tgagagtgga ttgcccagta cacgcattaa aaagagcaaa gctctttctg 840
gttttcagtct acaaagctgc aggcacagca tcccagtgtt ctgccattct tcatttttacc 900
atgacactga tttcttggga gaagaactgg atattgttgc tgcaaaaagt cacgaggcct 960
gccagaaact gtgcaccaat gccgtccgct gccagttttt tacctatacc ccagcccaag 1020
catcctgcaa cgaagggaag ggcaagtgtt acttaaagct ttcttcaaac ggatctccaa 1080
ctaaaatact tcacgggaga ggaggcatct ctggatacac attaaggttg tgtaaaatgg 1140
ataatgagtg taccaccaaa atcaagccca ggatcgttgg aggaactgcg tctgttcgtg 1200
gtgagtggcc gtggcaggtg accctgcaca caacctcacc cactcagaga cacctgtgtg 1260
gaggctccat cattggaaac cagtggatat taacagccgc tcactgtttc tatggggtag 1320
agtcacctaa gattttgcgt gtctacagtg gcattttaaa tcaatctgaa ataaaagagg 1380
acacatcttt ctttggggtt caagaaataa taatccatga tcagtataaa atggcagaaa 1440
gcgggtatga tattgccttg ttgaaactgg aaaccacagt gaattacaca gattctcaac 1500
gacccatatg cctgccttcc aaaggagata gaaatgtaat atacactgat tgctgggtga 1560
ctggatgggg gtacagaaaa ctaagagaca aaatacaaaa tactctccag aaagccaaga 1620
taccccttagt gaccaacgaa gagtgccaga agagatacag aggacataaa ataacccata 1680
agatgatctg tgccggctac agggaaggag ggaaggacgc ttgcaaggga gattcgggag 1740
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aaggctgtgc tcaaagggag cggccaggtg tttacaccaa cgtggtcgag tacgtggact 1860
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caagttgtta tgtcc 2055

<210> 196
<211> 571
<212> PRT
<213> Homo sapiens

<400> 196

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			20					25					30		
Gly	Asp	Ile	Thr	Thr	Val	Phe	Thr	Pro	Ser	Ala	Lys	Tyr	Cys	Gln	Val
		35					40					45			
Val	Cys	Thr	Tyr	His	Pro	Arg	Cys	Leu	Leu	Phe	Thr	Phe	Thr	Ala	Glu
	50					55					60				
Ser	Pro	Ser	Glu	Asp	Pro	Thr	Arg	Trp	Phe	Thr	Cys	Val	Leu	Lys	Asp
65					70					75					80
Ser	Val	Thr	Glu	Thr	Leu	Pro	Arg	Val	Asn	Arg	Thr	Ala	Ala	Ile	Ser
				85					90					95	
Gly	Tyr	Ser	Phe	Lys	Gln	Cys	Ser	His	Gln	Ile	Ser	Asn	Ile	Cys	Leu
			100					105					110		
Leu	Lys	His	Thr	Gln	Thr	Gly	Thr	Pro	Thr	Arg	Ile	Thr	Lys	Leu	Asp
		115					120					125			
Lys	Val	Val	Ser	Gly	Phe	Ser	Leu	Lys	Ser	Cys	Ala	Leu	Ser	Asn	Leu
	130					135					140				
Ala	Cys	Ile	Arg	Asp	Ile	Phe	Pro	Asn	Thr	Val	Phe	Ala	Asp	Ser	Asn
145					150					155					160
Ile	Asp	Ser	Val	Met	Ala	Pro	Asp	Ala	Phe	Val	Cys	Gly	Arg	Ile	Cys
				165					170					175	
Thr	His	His	Pro	Gly	Cys	Leu	Phe	Phe	Thr	Phe	Phe	Ser	Gln	Glu	Trp
			180					185					190		
Pro	Lys	Glu	Ser	Gln	Arg	Asn	Leu	Cys	Leu	Leu	Lys	Thr	Ser	Glu	Ser
		195					200					205			
Gly	Leu	Pro	Ser	Thr	Arg	Ile	Lys	Lys	Ser	Lys	Ala	Leu	Ser	Gly	Phe
	210					215					220				
Ser	Leu	Gln	Ser	Cys	Arg	His	Ser	Ile	Pro	Val	Phe	Cys	His	Ser	Ser
225					230					235					240
Phe	Tyr	His	Asp	Thr	Asp	Phe	Leu	Gly	Glu	Glu	Leu	Asp	Ile	Val	Ala
				245					250					255	
Ala	Lys	Ser	His	Glu	Ala	Cys	Gln	Lys	Leu	Cys	Thr	Asn	Ala	Val	Arg
			260					265					270		
Cys	Gln	Phe	Phe	Thr	Tyr	Thr	Pro	Ala	Gln	Ala	Ser	Cys	Asn	Glu	Gly
		275					280					285			
Lys	Gly	Lys	Cys	Tyr	Leu	Lys	Leu	Ser	Ser	Asn	Gly	Ser	Pro	Thr	Lys
	290					295					300				
Ile	Leu	His	Gly	Arg	Gly	Gly	Ile	Ser	Gly	Tyr	Thr	Leu	Arg	Leu	Cys
305					310					315					320
Lys	Met	Asp	Asn	Glu	Cys	Thr	Thr	Lys	Ile	Lys	Pro	Arg	Ile	Val	Gly
				325					330					335	
Gly	Thr	Ala	Ser	Val	Arg	Gly	Glu	Trp	Pro	Trp	Gln	Val	Thr	Leu	His
			340					345					350		
Thr	Thr	Ser	Pro	Thr	Gln	Arg	His	Leu	Cys	Gly	Gly	Ser	Ile	Ile	Gly

```
        355                 360                 365
Asn Gln Trp Ile Leu Thr Ala Ala His Cys Phe Tyr Gly Val Glu Ser
    370                 375                 380
Pro Lys Ile Leu Arg Val Tyr Ser Gly Ile Leu Asn Gln Ser Glu Ile
385                 390                 395                 400
Lys Glu Asp Thr Ser Phe Phe Gly Val Gln Glu Ile Ile Ile His Asp
                405                 410                 415
Gln Tyr Lys Met Ala Glu Ser Gly Tyr Asp Ile Ala Leu Leu Lys Leu
            420                 425                 430
Glu Thr Thr Val Asn Tyr Thr Asp Ser Gln Arg Pro Ile Cys Leu Pro
        435                 440                 445
Ser Lys Gly Asp Arg Asn Val Ile Tyr Thr Asp Cys Trp Val Thr Gly
    450                 455                 460
Trp Gly Tyr Arg Lys Leu Arg Asp Lys Ile Gln Asn Thr Leu Gln Lys
465                 470                 475                 480
Ala Lys Ile Pro Leu Val Thr Asn Glu Glu Cys Gln Lys Arg Tyr Arg
                485                 490                 495
Gly His Lys Ile Thr His Lys Met Ile Cys Ala Gly Tyr Arg Glu Gly
            500                 505                 510
Gly Lys Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Ser Cys Lys
        515                 520                 525
His Asn Glu Val Trp His Leu Val Gly Ile Thr Ser Trp Gly Glu Gly
    530                 535                 540
Cys Ala Gln Arg Glu Arg Pro Gly Val Tyr Thr Asn Val Val Glu Tyr
545                 550                 555                 560
Val Asp Trp Ile Leu Glu Lys Thr Gln Ala Val
                565                 570
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<210> 197
<211> 2804
<212> DNA
<213> Homo sapiens

<400> 197

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caccaggcct catcaccatc tgccttttag gatatctact cagtgctgaa tgtacagttt 120
ttcttgatca tgaaaacgcc aacaaaattc tgaatcggcc aaagaggtat aattcaggta 180
aattggaaga gtttgttcaa gggaaccttg agagagaatg tatggaagaa aagtgtagtt 240
ttgaagaagc acgagaagtt tttgaaaaca ctgaaagaac aactgaattt tggaagcagt 300
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acattaattc ctatgaatgt tggtgtccct ttggatttga aggaaagaac tgtgaattag 420
atgtaacatg taacattaag aatggcagat gcgagcagtt ttgtaaaaat agtgctgata 480
acaaggtggt ttgctcctgt actgagggat atcgacttgc agaaaaccag aagtcctgtg 540
aaccagcagt gccatttcca tgtggaagag tttctgtttc acaaacttct aagctcaccc 600
gtgctgagac tgtttttcct gatgtggact atgtaaattc tactgaagct gaaaccattt 660
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attttgatta tagttaatcc ttctatcttg aatcttctag agagttgctg accaactgac 2760
gtatgtttcc ctttgtgaat taataaactg gtgttctggt tcat                  2804
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<210> 198
<211> 461
<212> PRT
<213> Homo sapiens

<400> 198

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            20                  25                  30
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45
Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60
Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80
Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110
Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125
Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140
Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160
Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190
Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205
Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
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    210                 215                 220
Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240
Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile
                245                 250                 255
Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270
Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
        275                 280                 285
His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300
Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320
Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335
Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr
            340                 345                 350
Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365
Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg
    370                 375                 380
Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400
Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415
Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430
Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445
Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr
    450                 455                 460
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<210> 199
<211> 2478
<212> DNA
<213> Homo sapiens

<400> 199

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<211> 466
<212> PRT
<213> Homo sapiens

<400> 200
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Arg Asp Met Pro Trp Lys Pro Gly Pro His Arg Val Phe Val Thr Gln
        35   40   45
Glu Glu Ala His Gly Val Leu His Arg Arg Arg Arg Ala Asn Ala Phe
    50   55   60
Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu
65   70   75   80
Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg
                85   90   95
Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser
            100   105   110
Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr
        115   120   125
Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys Glu Thr His
    130   135   140
Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly Cys Glu Gln
145   150   155   160
Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu
                165   170   175
Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu
            180   185   190
Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys
        195   200   205
Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys
    210   215   220

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Pro Trp Gln Val Leu Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly
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Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp
                245                 250                 255
Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp
            260                 265                 270
Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gln Val
        275                 280                 285
Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala
    290                 295                 300
Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro
305                 310                 315                 320
Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val
                325                 330                 335
Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala
            340                 345                 350
Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln
        355                 360                 365
Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr
    370                 375                 380
Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys
385                 390                 395                 400
Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp
                405                 410                 415
Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly
            420                 425                 430
His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln
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Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro
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Phe Pro
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<210> 201
<211> 2412
<212> DNA
<213> Homo sapiens

<400> 201

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<210> 202
<211> 444
<212> PRT
<213> Homo sapiens

<400> 202

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			20					25					30		
Leu	His	Arg	Arg	Arg	Arg	Ala	Asn	Ala	Phe	Leu	Glu	Glu	Leu	Arg	Pro
		35					40					45			
Gly	Ser	Leu	Glu	Arg	Glu	Cys	Lys	Glu	Glu	Gln	Cys	Ser	Phe	Glu	Glu
	50					55					60				
Ala	Arg	Glu	Ile	Phe	Lys	Asp	Ala	Glu	Arg	Thr	Lys	Leu	Phe	Trp	Ile
65					70					75					80
Ser	Tyr	Ser	Asp	Gly	Asp	Gln	Cys	Ala	Ser	Ser	Pro	Cys	Gln	Asn	Gly
				85					90					95	
Gly	Ser	Cys	Lys	Asp	Gln	Leu	Gln	Ser	Tyr	Ile	Cys	Phe	Cys	Leu	Pro
			100					105					110		
Ala	Phe	Glu	Gly	Arg	Asn	Cys	Glu	Thr	His	Lys	Asp	Asp	Gln	Leu	Ile
		115					120					125			
Cys	Val	Asn	Glu	Asn	Gly	Gly	Cys	Glu	Gln	Tyr	Cys	Ser	Asp	His	Thr
	130					135					140				
Gly	Thr	Lys	Arg	Ser	Cys	Arg	Cys	His	Glu	Gly	Tyr	Ser	Leu	Leu	Ala
145					150					155					160
Asp	Gly	Val	Ser	Cys	Thr	Pro	Thr	Val	Glu	Tyr	Pro	Cys	Gly	Lys	Ile
				165					170					175	
Pro	Ile	Leu	Glu	Lys	Arg	Asn	Ala	Ser	Lys	Pro	Gln	Gly	Arg	Ile	Val
			180					185					190		
Gly	Gly	Lys	Val	Cys	Pro	Lys	Gly	Glu	Cys	Pro	Trp	Gln	Val	Leu	Leu
		195					200					205			
Leu	Val	Asn	Gly	Ala	Gln	Leu	Cys	Gly	Gly	Thr	Leu	Ile	Asn	Thr	Ile
	210					215					220				

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Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225                 230                 235                 240
Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
                245                 250                 255
Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
            260                 265                 270
Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
        275                 280                 285
Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg
    290                 295                 300
Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305                 310                 315                 320
Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
                325                 330                 335
Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
            340                 345                 350
Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
        355                 360                 365
Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
    370                 375                 380
Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385                 390                 395                 400
Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
                405                 410                 415
Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
            420                 425                 430
Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
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<210> 203
<211> 1502
<212> DNA
<213> Homo sapiens

<400> 203

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tc 1502

<210> 204
<211> 488
<212> PRT
<213> Homo sapiens

<400> 204

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			20					25					30		
Asn	Ile	Leu	Ala	Arg	Val	Thr	Arg	Ala	Asn	Ser	Phe	Leu	Glu	Glu	Met
		35					40					45			
Lys	Lys	Gly	His	Leu	Glu	Arg	Glu	Cys	Met	Glu	Glu	Thr	Cys	Ser	Tyr
	50					55					60				
Glu	Glu	Ala	Arg	Glu	Val	Phe	Glu	Asp	Ser	Asp	Lys	Thr	Asn	Glu	Phe
65					70					75					80
Trp	Asn	Lys	Tyr	Lys	Asp	Gly	Asp	Gln	Cys	Glu	Thr	Ser	Pro	Cys	Gln
				85					90					95	
Asn	Gln	Gly	Lys	Cys	Lys	Asp	Gly	Leu	Gly	Glu	Tyr	Thr	Cys	Thr	Cys
			100					105					110		
Leu	Glu	Gly	Phe	Glu	Gly	Lys	Asn	Cys	Glu	Leu	Phe	Thr	Arg	Lys	Leu
		115					120					125			
Cys	Ser	Leu	Asp	Asn	Gly	Asp	Cys	Asp	Gln	Phe	Cys	His	Glu	Glu	Gln
	130					135					140				
Asn	Ser	Val	Val	Cys	Ser	Cys	Ala	Arg	Gly	Tyr	Thr	Leu	Ala	Asp	Asn
145					150					155					160
Gly	Lys	Ala	Cys	Ile	Pro	Thr	Gly	Pro	Tyr	Pro	Cys	Gly	Lys	Gln	Thr
				165					170					175	
Leu	Glu	Arg	Arg	Lys	Arg	Ser	Val	Ala	Gln	Ala	Thr	Ser	Ser	Ser	Gly
			180					185					190		
Glu	Ala	Pro	Asp	Ser	Ile	Thr	Trp	Lys	Pro	Tyr	Asp	Ala	Ala	Asp	Leu
		195					200					205			
Asp	Pro	Thr	Glu	Asn	Pro	Phe	Asp	Leu	Leu	Asp	Phe	Asn	Gln	Thr	Gln
	210					215					220				
Pro	Glu	Arg	Gly	Asp	Asn	Asn	Leu	Thr	Arg	Ile	Val	Gly	Gly	Gln	Glu
225					230					235					240
Cys	Lys	Asp	Gly	Glu	Cys	Pro	Trp	Gln	Ala	Leu	Leu	Ile	Asn	Glu	Glu
				245					250					255	
Asn	Glu	Gly	Phe	Cys	Gly	Gly	Thr	Ile	Leu	Ser	Glu	Phe	Tyr	Ile	Leu
			260					265					270		
Thr	Ala	Ala	His	Cys	Leu	Tyr	Gln	Ala	Lys	Arg	Phe	Lys	Val	Arg	Val
		275					280					285			
Gly	Asp	Arg	Asn	Thr	Glu	Gln	Glu	Glu	Gly	Gly	Glu	Ala	Val	His	Glu
	290					295					300				
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305					310					315					320
Phe	Asp	Ile	Ala	Val	Leu	Arg	Leu	Lys	Thr	Pro	Ile	Thr	Phe	Arg	Met
				325					330					335	
Asn	Val	Ala	Pro	Ala	Cys	Leu	Pro	Glu	Arg	Asp	Trp	Ala	Glu	Ser	Thr
			340					345					350		
Leu	Met	Thr	Gln	Lys	Thr	Gly	Ile	Val	Ser	Gly	Phe	Gly	Arg	Thr	His
		355					360					365			
Glu	Lys	Gly	Arg	Gln	Ser	Thr	Arg	Leu	Lys	Met	Leu	Glu	Val	Pro	Tyr

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385                 390                 395                 400
Asn Met Phe Cys Ala Gly Tyr Asp Thr Lys Gln Glu Asp Ala Cys Gln
                405                 410                 415
Gly Asp Ser Gly Gly Pro His Val Thr Arg Phe Lys Asp Thr Tyr Phe
            420                 425                 430
Val Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Arg Lys Gly Lys
        435                 440                 445
Tyr Gly Ile Tyr Thr Lys Val Thr Ala Phe Leu Lys Trp Ile Asp Arg
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Val Ile Thr Ser Ser Pro Leu Lys
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<210> 205
<211> 1997
<212> DNA
<213> Homo sapiens

<400> 205

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aaccgaaaga gagctcctgg aatcctacat cgacgggcgc attgtggagg gctcggatgc 1140
agagatcggc atgtcacctt ggcaggtgat gcttttccgg aagagtcccc aggagctgct 1200
gtgtggggcc agcctcatca gtgaccgctg ggtcctcacc gccgcccact gcctcctgta 1260
cccgccctgg gacaagaact tcaccgagaa tgaccttctg gtgcgcattg gcaagcactc 1320
ccgcacaagg tacgagcgaa acattgaaaa gatatccatg ttggaaaaga tctacatcca 1380
ccccaggtac aactggcggg agaacctgga ccgggacatt gccctgatga agctgaagaa 1440
gcctgttgcc ttcagtgact acattcaccc tgtgtgtctg cccgacaggg agacggcagc 1500
cagcttgctc caggctggat acaaggggcg ggtgacaggc tggggcaacc tgaaggagac 1560
gtggacagcc aacgttggta aggggcagcc cagtgtcctg caggtggtga acctgcccat 1620
tgtggagcgg ccggtctgca aggactccac ccggatccgc atcactgaca acatgttctg 1680
tgctggttac aagcctgatg aagggaaacg aggggatgcc tgtgaaggtg acagtggggg 1740
acccttttgtc atgaagagcc cctttaacaa ccgctggtat caaatgggca tcgtctcatg 1800
gggtgaaggc tgtgaccggg atgggaaata tggcttctac acacatgtgt tccgcctgaa 1860
gaagtggata cagaaggtca ttgatcagtt tggagagtag gggccactca tattctgggc 1920
tcctggaacc aatcccgtga aagaattatt tttgtgtttc taaaactatg gttcccaata 1980
aaagtgactc tcagcgg                                                1997
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<210> 206
<211> 622
<212> PRT
<213> Homo sapiens

<400> 206

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 1               5                  10                  15
Ala Leu Cys Ser Leu Val His Ser Gln His Val Phe Leu Ala Pro Gln
            20                  25                  30
Gln Ala Arg Ser Leu Leu Gln Arg Val Arg Arg Ala Asn Thr Phe Leu
        35                  40                  45
Glu Glu Val Arg Lys Gly Asn Leu Glu Arg Glu Cys Val Glu Glu Thr
    50                  55                  60
Cys Ser Tyr Glu Glu Ala Phe Glu Ala Leu Glu Ser Ser Thr Ala Thr
65                  70                  75                  80
Asp Val Phe Trp Ala Lys Tyr Thr Ala Cys Glu Thr Ala Arg Thr Pro
                85                  90                  95
Arg Asp Lys Leu Ala Ala Cys Leu Glu Gly Asn Cys Ala Glu Gly Leu
            100                 105                 110
Gly Thr Asn Tyr Arg Gly His Val Asn Ile Thr Arg Ser Gly Ile Glu
        115                 120                 125
Cys Gln Leu Trp Arg Ser Arg Tyr Pro His Lys Pro Glu Ile Asn Ser
    130                 135                 140
Thr Thr His Pro Gly Ala Asp Leu Gln Glu Asn Phe Cys Arg Asn Pro
145                 150                 155                 160
Asp Ser Ser Thr Thr Gly Pro Trp Cys Tyr Thr Thr Asp Pro Thr Val
                165                 170                 175
Arg Arg Gln Glu Cys Ser Ile Pro Val Cys Gly Gln Asp Gln Val Thr
            180                 185                 190
Val Ala Met Thr Pro Arg Ser Glu Gly Ser Ser Val Asn Leu Ser Pro
        195                 200                 205
Pro Leu Glu Gln Cys Val Pro Asp Arg Gly Gln Gln Tyr Gln Gly Arg
    210                 215                 220
Leu Ala Val Thr Thr His Gly Leu Pro Cys Leu Ala Trp Ala Ser Ala
225                 230                 235                 240
Gln Ala Lys Ala Leu Ser Lys His Gln Asp Phe Asn Ser Ala Val Gln
                245                 250                 255
Leu Val Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Glu Glu Gly Val
            260                 265                 270
Trp Cys Tyr Val Ala Gly Lys Pro Gly Asp Phe Gly Tyr Cys Asp Leu
        275                 280                 285
Asn Tyr Cys Glu Glu Ala Val Glu Glu Glu Thr Gly Asp Gly Leu Asp
    290                 295                 300
Glu Asp Ser Asp Arg Ala Ile Glu Gly Arg Thr Ala Thr Ser Glu Tyr
305                 310                 315                 320
Gln Thr Phe Phe Asn Pro Arg Thr Phe Gly Ser Gly Glu Ala Asp Cys
                325                 330                 335
Gly Leu Arg Pro Leu Phe Glu Lys Lys Ser Leu Glu Asp Lys Thr Glu
            340                 345                 350
Arg Glu Leu Leu Glu Ser Tyr Ile Asp Gly Arg Ile Val Glu Gly Ser
        355                 360                 365
Asp Ala Glu Ile Gly Met Ser Pro Trp Gln Val Met Leu Phe Arg Lys
    370                 375                 380
Ser Pro Gln Glu Leu Leu Cys Gly Ala Ser Leu Ile Ser Asp Arg Trp
385                 390                 395                 400
Val Leu Thr Ala Ala His Cys Leu Leu Tyr Pro Pro Trp Asp Lys Asn
                405                 410                 415
```

```
Phe Thr Glu Asn Asp Leu Leu Val Arg Ile Gly Lys His Ser Arg Thr
            420                 425                 430
Arg Tyr Glu Arg Asn Ile Glu Lys Ile Ser Met Leu Glu Lys Ile Tyr
        435                 440                 445
Ile His Pro Arg Tyr Asn Trp Arg Glu Asn Leu Asp Arg Asp Ile Ala
    450                 455                 460
Leu Met Lys Leu Lys Lys Pro Val Ala Phe Ser Asp Tyr Ile His Pro
465                 470                 475                 480
Val Cys Leu Pro Asp Arg Glu Thr Ala Ala Ser Leu Leu Gln Ala Gly
                485                 490                 495
Tyr Lys Gly Arg Val Thr Gly Trp Gly Asn Leu Lys Glu Thr Trp Thr
            500                 505                 510
Ala Asn Val Gly Lys Gly Gln Pro Ser Val Leu Gln Val Val Asn Leu
        515                 520                 525
Pro Ile Val Glu Arg Pro Val Cys Lys Asp Ser Thr Arg Ile Arg Ile
    530                 535                 540
Thr Asp Asn Met Phe Cys Ala Gly Tyr Lys Pro Asp Glu Gly Lys Arg
545                 550                 555                 560
Gly Asp Ala Cys Glu Gly Asp Ser Gly Gly Pro Phe Val Met Lys Ser
                565                 570                 575
Pro Phe Asn Asn Arg Trp Tyr Gln Met Gly Ile Val Ser Trp Gly Glu
            580                 585                 590
Gly Cys Asp Arg Asp Gly Lys Tyr Gly Phe Tyr Thr His Val Phe Arg
        595                 600                 605
Leu Lys Lys Trp Ile Gln Lys Val Ile Asp Gln Phe Gly Glu
    610                 615                 620
```

<210> 207
<211> 1843
<212> DNA
<213> Homo sapiens

<400> 207

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ctgcaggggg ggggggggag gggggctgtc atggcggcag gacggcgaac ttgcagtatc 60
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gctgttcgtg gccacctggg gaatttccgg cacaccagct cctcttgact cagtgttctc 180
cagcagcgag cgtgcccacc aggtgctgcg gatccgcaaa cgtgccaact ccttcctgga 240
ggagctccgt cacagcagcc tggagcggga gtgcatagag gagatctgtg acttcgagga 300
ggccaaggaa attttccaaa atgtggatga cacactggcc ttctggtcca agcacgtcga 360
cggtgaccag tgcttggtct tgcccttgga gcacccgtgc gccagcctgt gctgcgggca 420
cggcacgtgc atcgacggca tcggcagctt cagctgcgac tgccgcagcg gctgggaggg 480
ccgcttctgc cagcgcgagg tgagcttcct caattgctcg ctggacaacg gcggctgcac 540
gcattactgc ctagaggagg tgggctggcg gcgctgtagc tgtgcgcctg gctacaagct 600
gggggacgac ctcctgcagt gtcaccccgc agtgaagttc ccttgtggga ggccctggaa 660
gcggatggag aagaagcgca gtcacctgaa acgagacaca gaagaccaag aagaccaagt 720
agatccgcgg ctcattgatg ggaagatgac caggcgggga gacagcccct ggcaggtggt 780
cctgctggac tcaaagaaga agctggcctg cggggcagtg ctcatccacc cctcctgggt 840
gctgacagcg gcccactgca tggatgagtc caagaagctc cttgtcaggc ttggagagta 900
tgacctgcgg cgctgggaga agtgggagct ggacctggac atcaaggagg tcttcgtcca 960
ccccaactac agcaagagca ccaccgacaa tgacatcgca ctgctgcacc tggcccagcc 1020
cgccaccctc tcgcagacca tagtgcccat ctgcctcccg gacagcggcc ttgcagagcg 1080
cgagctcaat caggccggcc aggagaccct cgtgacgggc tggggctacc acagcagccg 1140
agagaaggag gccaagagaa accgcacctt cgtcctcaac ttcatcaaga ttcccgtggt 1200
cccgcacaat gagtgcagcg aggtcatgag caacatggtg tctgagaaca tgctgtgtgc 1260
gggcatcctc ggggaccggc aggatgcctg cgagggcgac agtgggggggc ccatggtcgc 1320
ctccttccac ggcacctggt tcctggtggg cctggtgagc tggggtgagg gctgtgggct 1380
ccttcacaac tacggcgttt acaccaaagt cagccgctac ctcgactgga tccatgggca 1440
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catcagagac aaggaagccc cccagaagag ctgggcacct tagcgaccct ccctgcaggg 1500
ctgggctttt gcatggcaat ggatgggaca ttaaagggac atgtaacaag cacaccggcc 1560
tgctgttctg tccttccatc cctcttttgg gctcttctgg agggaagtaa catttactga 1620
gcacctgttg tatgtcacat gccttatgaa tagaatctta actcctagag caactctgtg 1680
gggtggggag gagcagatcc aagttttgcg gggtctaaag ctgtgtgtgt tgagggggat 1740
actctgttta tgaaaaagaa taaaaaacac aaccacgaaa aaaaaaaaaa aaaaaaaaaa 1800
aaaaaaaaaa aaaaaaaccc ccccccgccc ccccccccctg cag 1843

<210> 208
<211> 461
<212> PRT
<213> Homo sapiens

<400> 208

Met	Trp	Gln	Leu	Thr	Ser	Leu	Leu	Leu	Phe	Val	Ala	Thr	Trp	Gly	Ile
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Ser	Gly	Thr	Pro	Ala	Pro	Leu	Asp	Ser	Val	Phe	Ser	Ser	Ser	Glu	Arg
			20					25				30			
Ala	His	Gln	Val	Leu	Arg	Ile	Arg	Lys	Arg	Ala	Asn	Ser	Phe	Leu	Glu
		35					40					45			
Glu	Leu	Arg	His	Ser	Ser	Leu	Glu	Arg	Glu	Cys	Ile	Glu	Glu	Ile	Cys
	50					55					60				
Asp	Phe	Glu	Glu	Ala	Lys	Glu	Ile	Phe	Gln	Asn	Val	Asp	Asp	Thr	Leu
65					70					75					80
Ala	Phe	Trp	Ser	Lys	His	Val	Asp	Gly	Asp	Gln	Cys	Leu	Val	Leu	Pro
				85					90					95	
Leu	Glu	His	Pro	Cys	Ala	Ser	Leu	Cys	Cys	Gly	His	Gly	Thr	Cys	Ile
			100					105					110		
Asp	Gly	Ile	Gly	Ser	Phe	Ser	Cys	Asp	Cys	Arg	Ser	Gly	Trp	Glu	Gly
		115					120					125			
Arg	Phe	Cys	Gln	Arg	Glu	Val	Ser	Phe	Leu	Asn	Cys	Ser	Leu	Asp	Asn
	130					135					140				
Gly	Gly	Cys	Thr	His	Tyr	Cys	Leu	Glu	Glu	Val	Gly	Trp	Arg	Arg	Cys
145					150					155					160
Ser	Cys	Ala	Pro	Gly	Tyr	Lys	Leu	Gly	Asp	Asp	Leu	Leu	Gln	Cys	His
				165					170					175	
Pro	Ala	Val	Lys	Phe	Pro	Cys	Gly	Arg	Pro	Trp	Lys	Arg	Met	Glu	Lys
			180					185					190		
Lys	Arg	Ser	His	Leu	Lys	Arg	Asp	Thr	Glu	Asp	Gln	Glu	Asp	Gln	Val
		195					200					205			
Asp	Pro	Arg	Leu	Ile	Asp	Gly	Lys	Met	Thr	Arg	Arg	Gly	Asp	Ser	Pro
	210					215					220				
Trp	Gln	Val	Val	Leu	Leu	Asp	Ser	Lys	Lys	Lys	Leu	Ala	Cys	Gly	Ala
225					230					235					240
Val	Leu	Ile	His	Pro	Ser	Trp	Val	Leu	Thr	Ala	Ala	His	Cys	Met	Asp
				245					250					255	
Glu	Ser	Lys	Lys	Leu	Leu	Val	Arg	Leu	Gly	Glu	Tyr	Asp	Leu	Arg	Arg
			260					265					270		
Trp	Glu	Lys	Trp	Glu	Leu	Asp	Leu	Asp	Ile	Lys	Glu	Val	Phe	Val	His
		275					280					285			
Pro	Asn	Tyr	Ser	Lys	Ser	Thr	Thr	Asp	Asn	Asp	Ile	Ala	Leu	Leu	His
	290					295					300				
Leu	Ala	Gln	Pro	Ala	Thr	Leu	Ser	Gln	Thr	Ile	Val	Pro	Ile	Cys	Leu
305					310					315					320
Pro	Asp	Ser	Gly	Leu	Ala	Glu	Arg	Glu	Leu	Asn	Gln	Ala	Gly	Gln	Glu
				325					330					335	
Thr	Leu	Val	Thr	Gly	Trp	Gly	Tyr	His	Ser	Ser	Arg	Glu	Lys	Glu	Ala
			340					345					350		

```
Lys Arg Asn Arg Thr Phe Val Leu Asn Phe Ile Lys Ile Pro Val Val
        355                 360                 365
Pro His Asn Glu Cys Ser Glu Val Met Ser Asn Met Val Ser Glu Asn
    370                 375                 380
Met Leu Cys Ala Gly Ile Leu Gly Asp Arg Gln Asp Ala Cys Glu Gly
385                 390                 395                 400
Asp Ser Gly Gly Pro Met Val Ala Ser Phe His Gly Thr Trp Phe Leu
                405                 410                 415
Val Gly Leu Val Ser Trp Gly Glu Gly Cys Gly Leu Leu His Asn Tyr
            420                 425                 430
Gly Val Tyr Thr Lys Val Ser Arg Tyr Leu Asp Trp Ile His Gly His
        435                 440                 445
Ile Arg Asp Lys Glu Ala Pro Gln Lys Ser Trp Ala Pro
    450                 455                 460
```

<210> 209
<211> 1388
<212> DNA
<213> Homo sapiens

<400> 209

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gtccgtggtt gctaaagata acgccacgtg tgatggcccc tgtgggttac ggttcaggca 120
aaacccacag ggtggtgtcc gcatcgtcgg cgggaaggct gcacagcatg gggcctggcc 180
ctggatggtc agcctccaga tcttcacgta caacagccac aggtaccaca catgtggagg 240
cagcttgctg aattcacgat gggtgctcac tgctgctcac tgcttcgtcg gcaaaaataa 300
tgtgcatgac tggagactgg ttttcggagc aaaggaaatt acatatggga acaataaacc 360
agtaaaggcg cctgtgcaag agagatatgt ggagaaaatc atcattcatg aaaaatacaa 420
ctctgcgaca gagggaaatg acattgccct cgtggagatc acccctccca tttcgtgtgg 480
gcgcttcatt gggccgggct gcctgcccca cttgaaggca ggcctcccca gaggctccca 540
gagctgctgg gtggccggct ggggatatat agaagagaaa gcccccaggc catcatctat 600
actgatggag gcacgtgtgg atctcatcga cctggacttg tgtaactcga cccagtggta 660
caatgggcgc gttcagccaa ccaatgtgtg cgcggggtat cctgtaggca agatcgacac 720
ctgccaggga gacagcggcg ggcctctcat gtgcaaagac agcaaggaaa gcgcctatgt 780
ggtcgtggga atcacaagct ggggggtagg ctgtgcccgt gccaagcgcc ccggaatcta 840
cacggccacc tggccttatc tgaactggat cgcctccaag attggttcta acgctttgcg 900
tatgattcaa tcggccaccc ctccaccgcc caccactcga ccgcccccga ttcgaccccc 960
cttctcccac cctatctctg ctcaccttcc ttggtatttc caaccgcccc ctcgaccact 1020
tccaccccga ccaccggcag cccagccccg acccccacct tcaccccccgc ccccaccccc 1080
acctccagcc tcacctttac ccccaccccc acccccaccc ccacctacac cctcatctac 1140
cacaaaactt ccccaaggac tttcttttgc caagcgccta cagcagctca tagaggtctt 1200
gaaggggaag acctattccg acggaaagaa ccattatgac atggagacca cagagctccc 1260
agaactgacc tcgacctcct gatctgacct ggttctcaac agacccagtg agcccttcac 1320
tcctgagaaa aaggaaagat gaaataaata aataaacata tatatataga tataaaaaaa 1380
aaaaaaaa                                                        1388
```

<210> 210
<211> 421
<212> PRT
<213> Homo sapiens

<400> 210

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Met Val Glu Met Leu Pro Thr Ala Ile Leu Leu Val Leu Ala Val Ser
 1               5                  10                  15
Val Val Ala Lys Asp Asn Ala Thr Cys Asp Gly Pro Cys Gly Leu Arg
            20                  25                  30
Phe Arg Gln Asn Pro Gln Gly Gly Val Arg Ile Val Gly Gly Lys Ala
```

```
        35                  40                  45
Ala Gln His Gly Ala Trp Pro Trp Met Val Ser Leu Gln Ile Phe Thr
    50                  55                  60
Tyr Asn Ser His Arg Tyr His Thr Cys Gly Gly Ser Leu Leu Asn Ser
65                  70                  75                  80
Arg Trp Val Leu Thr Ala Ala His Cys Phe Val Gly Lys Asn Asn Val
                85                  90                  95
His Asp Trp Arg Leu Val Phe Gly Ala Lys Glu Ile Thr Tyr Gly Asn
            100                 105                 110
Asn Lys Pro Val Lys Ala Pro Val Gln Glu Arg Tyr Val Glu Lys Ile
        115                 120                 125
Ile Ile His Glu Lys Tyr Asn Ser Ala Thr Glu Gly Asn Asp Ile Ala
    130                 135                 140
Leu Val Glu Ile Thr Pro Pro Ile Ser Cys Gly Arg Phe Ile Gly Pro
145                 150                 155                 160
Gly Cys Leu Pro His Leu Lys Ala Gly Leu Pro Arg Gly Ser Gln Ser
                165                 170                 175
Cys Trp Val Ala Gly Trp Gly Tyr Ile Glu Glu Lys Ala Pro Arg Pro
            180                 185                 190
Ser Ser Ile Leu Met Glu Ala Arg Val Asp Leu Ile Asp Leu Asp Leu
        195                 200                 205
Cys Asn Ser Thr Gln Trp Tyr Asn Gly Arg Val Gln Pro Thr Asn Val
    210                 215                 220
Cys Ala Gly Tyr Pro Val Gly Lys Ile Asp Thr Cys Gln Gly Asp Ser
225                 230                 235                 240
Gly Gly Pro Leu Met Cys Lys Asp Ser Lys Glu Ser Ala Tyr Val Val
                245                 250                 255
Val Gly Ile Thr Ser Trp Gly Val Gly Cys Ala Arg Ala Lys Arg Pro
            260                 265                 270
Gly Ile Tyr Thr Ala Thr Trp Pro Tyr Leu Asn Trp Ile Ala Ser Lys
        275                 280                 285
Ile Gly Ser Asn Ala Leu Arg Met Ile Gln Ser Ala Thr Pro Pro Pro
    290                 295                 300
Pro Thr Thr Arg Pro Pro Pro Ile Arg Pro Pro Phe Ser His Pro Ile
305                 310                 315                 320
Ser Ala His Leu Pro Trp Tyr Phe Gln Pro Pro Pro Arg Pro Leu Pro
                325                 330                 335
Pro Arg Pro Pro Ala Ala Gln Pro Arg Pro Pro Pro Ser Pro Pro Pro
            340                 345                 350
Pro Pro Pro Pro Pro Ala Ser Pro Leu Pro Pro Pro Pro Pro Pro Pro
        355                 360                 365
Pro Pro Thr Pro Ser Ser Thr Thr Lys Leu Pro Gln Gly Leu Ser Phe
    370                 375                 380
Ala Lys Arg Leu Gln Gln Leu Ile Glu Val Leu Lys Gly Lys Thr Tyr
385                 390                 395                 400
Ser Asp Gly Lys Asn His Tyr Asp Met Glu Thr Thr Glu Leu Pro Glu
                405                 410                 415
Leu Thr Ser Thr Ser
            420
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<210> 211
<211> 2363
<212> DNA
<213> Homo sapiens

<400> 211
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tgcccaggcc tggagactga cccgaccccg gcactacctc gaggctccgc ccccacctgc 180
tggaccccag ggtaaggaca agggcccccа gactcacagt tccagccctg aggacagggg 240
ttccctcatc cccccaccca gcctaatgcc cacctcctaa tagaggggtt cctggggacc 300
tgaagagggg gcactatgac gtctccccaa gcacctaggt gttctgtcct gctcttcctt 360
cagactcagc cgttggaccc cagtcctttc ctccccagac ccaggagttc cagccctcag 420
gcccctcctc cctcatacta gggagtcctg gcccccaaat tcctcctttc ccaagactta 480
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caggctcagg catgggggtc cccatcctg caaatccagg cgtccccccg ctgctggtca 600
gacactgacc ccatccttga acccagccca atctgcgtcc gtgatcacgg cgtgctctgg 660
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aagccaggcg tctacaccaa agtcagtgac ttccgggagt ggatcttcca ggccataaag 2040
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cacagtggcg ggcccactca gccccgagac cacccaacct caccctcctg acccccatgt 2280
aaatattgtt ctgctgtctg ggactcctgt ctaggtgccc ctgatgatgg gatgctcttt 2340
aaataataaa gatggttttg att                                        2363
```

<210> 212
<211> 417
<212> PRT
<213> Homo sapiens

<400> 212

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Met Ala Gln Lys Glu Gly Gly Arg Thr Val Pro Cys Cys Ser Arg Pro
 1               5                  10                  15
Lys Val Ala Ala Leu Thr Ala Gly Thr Leu Leu Leu Leu Thr Ala Ile
            20                  25                  30
Gly Ala Ala Ser Trp Ala Ile Val Ala Val Leu Leu Arg Ser Asp Gln
        35                  40                  45
Glu Pro Leu Tyr Pro Val Gln Val Ser Ser Ala Asp Ala Arg Leu Met
    50                  55                  60
Val Phe Asp Lys Thr Glu Gly Thr Trp Arg Leu Leu Cys Ser Ser Arg
65                  70                  75                  80
Ser Asn Ala Arg Val Ala Gly Leu Ser Cys Glu Glu Met Gly Phe Leu
                85                  90                  95
```

```
Arg Ala Leu Thr His Ser Glu Leu Asp Val Arg Thr Ala Gly Ala Asn
            100                 105                 110
Gly Thr Ser Gly Phe Phe Cys Val Asp Glu Gly Arg Leu Pro His Thr
        115                 120                 125
Gln Arg Leu Leu Glu Val Ile Ser Val Cys Asp Cys Pro Arg Gly Arg
    130                 135                 140
Phe Leu Ala Ala Ile Cys Gln Asp Cys Gly Arg Arg Lys Leu Pro Val
145                 150                 155                 160
Asp Arg Ile Val Gly Gly Arg Asp Thr Ser Leu Gly Arg Trp Pro Trp
                165                 170                 175
Gln Val Ser Leu Arg Tyr Asp Gly Ala His Leu Cys Gly Gly Ser Leu
            180                 185                 190
Leu Ser Gly Asp Trp Val Leu Thr Ala Ala His Cys Phe Pro Glu Arg
        195                 200                 205
Asn Arg Val Leu Ser Arg Trp Arg Val Phe Ala Gly Ala Val Ala Gln
    210                 215                 220
Ala Ser Pro His Gly Leu Gln Leu Gly Val Gln Ala Val Val Tyr His
225                 230                 235                 240
Gly Gly Tyr Leu Pro Phe Arg Asp Pro Asn Ser Glu Glu Asn Ser Asn
                245                 250                 255
Asp Ile Ala Leu Val His Leu Ser Ser Pro Leu Pro Leu Thr Glu Tyr
            260                 265                 270
Ile Gln Pro Val Cys Leu Pro Ala Ala Gly Gln Ala Leu Val Asp Gly
        275                 280                 285
Lys Ile Cys Thr Val Thr Gly Trp Gly Asn Thr Gln Tyr Tyr Gly Gln
    290                 295                 300
Gln Ala Gly Val Leu Gln Glu Ala Arg Val Pro Ile Ile Ser Asn Asp
305                 310                 315                 320
Val Cys Asn Gly Ala Asp Phe Tyr Gly Asn Gln Ile Lys Pro Lys Met
                325                 330                 335
Phe Cys Ala Gly Tyr Pro Glu Gly Gly Ile Asp Ala Cys Gln Gly Asp
            340                 345                 350
Ser Gly Gly Pro Phe Val Cys Glu Asp Ser Ile Ser Arg Thr Pro Arg
        355                 360                 365
Trp Arg Leu Cys Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu Ala
    370                 375                 380
Gln Lys Pro Gly Val Tyr Thr Lys Val Ser Asp Phe Arg Glu Trp Ile
385                 390                 395                 400
Phe Gln Ala Ile Lys Thr His Ser Glu Ala Ser Gly Met Val Thr Gln
                405                 410                 415
Leu
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<210> 213
<211> 1783
<212> DNA
<213> Homo sapiens

<400> 213
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tggaccccag ggtcccaccc tggcccagga ggtcagccag ggaatcatta acaagaggca 240
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cggacgctcg gctcatggtc tttgacaaga cggaagggac gtggcggctg ctgtgctcct 480

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<210> 214
<211> 417
<212> PRT
<213> Homo sapiens

<400> 214
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            20   25   30
Gly Ala Ala Ser Trp Ala Ile Val Ala Val Leu Leu Arg Ser Asp Gln
        35   40   45
Glu Pro Leu Tyr Pro Val Gln Val Ser Ser Ala Asp Ala Arg Leu Met
    50   55   60
Val Phe Asp Lys Thr Glu Gly Thr Trp Arg Leu Leu Cys Ser Ser Arg
65   70   75   80
Ser Asn Ala Arg Val Ala Gly Leu Ser Cys Glu Glu Met Gly Phe Leu
                85   90   95
Arg Ala Leu Thr His Ser Glu Leu Asp Val Arg Thr Ala Gly Ala Asn
            100   105   110
Gly Thr Ser Gly Phe Phe Cys Val Asp Glu Gly Arg Leu Pro His Thr
        115   120   125
Gln Arg Leu Leu Glu Val Ile Ser Val Cys Asp Cys Pro Arg Gly Arg
    130   135   140
Phe Leu Ala Ala Ile Cys Gln Asp Cys Gly Arg Arg Lys Leu Pro Val
145   150   155   160
Asp Arg Ile Val Gly Gly Arg Asp Thr Ser Leu Gly Arg Trp Pro Trp
                165   170   175
Gln Val Ser Leu Arg Tyr Asp Gly Ala His Leu Cys Gly Gly Ser Leu
            180   185   190
Leu Ser Gly Asp Trp Val Leu Thr Ala Ala His Cys Phe Pro Glu Arg
        195   200   205
Asn Arg Val Leu Ser Arg Trp Arg Val Phe Ala Gly Ala Val Ala Gln
    210   215   220
Ala Ser Pro His Gly Leu Gln Leu Gly Val Gln Ala Val Val Tyr His

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225                 230                 235                 240
Gly Gly Tyr Leu Pro Phe Arg Asp Pro Asn Ser Glu Glu Asn Ser Asn
                245                 250                 255
Asp Ile Ala Leu Val His Leu Ser Ser Pro Leu Pro Leu Thr Glu Tyr
            260                 265                 270
Ile Gln Pro Val Cys Leu Pro Ala Ala Gly Gln Ala Leu Val Asp Gly
        275                 280                 285
Lys Ile Cys Thr Val Thr Gly Trp Gly Asn Thr Gln Tyr Tyr Gly Gln
    290                 295                 300
Gln Ala Gly Val Leu Gln Glu Ala Arg Val Pro Ile Ile Ser Asn Asp
305                 310                 315                 320
Val Cys Asn Gly Ala Asp Phe Tyr Gly Asn Gln Ile Lys Pro Lys Met
                325                 330                 335
Phe Cys Ala Gly Tyr Pro Glu Gly Gly Ile Asp Ala Cys Gln Gly Asp
            340                 345                 350
Ser Gly Gly Pro Phe Val Cys Glu Asp Ser Ile Ser Arg Thr Pro Arg
        355                 360                 365
Trp Arg Leu Cys Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu Ala
    370                 375                 380
Gln Lys Pro Gly Val Tyr Thr Lys Val Ser Asp Phe Arg Glu Trp Ile
385                 390                 395                 400
Phe Gln Ala Ile Lys Thr His Ser Glu Ala Ser Gly Met Val Thr Gln
                405                 410                 415
Leu
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<210> 215
<211> 2038
<212> DNA
<213> Homo sapiens

<400> 215

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gtgacctctg tgacctctga gaccccagca acaagtgctc cagaggcaga gggaccccaa 240
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gaccgggaca gggcctgggg ctactgtgtg gaggccaccc cgcctccagg gggcccagct 480
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gtggtgctgg gccagcactt cttcaaccgc acgacggacg tgacgcagac cttcggcatc 1440
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tggatcaacg accggatacg gcctcccagg cggcttgtgg ctccctcctg accctccagc 1980
gggacaccct ggttcccacc attccctgcc ttgctgacaa taaagatatt tccaagaa 2038

<210> 216
<211> 655
<212> PRT
<213> Homo sapiens

<400> 216

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Gly	Pro	Phe	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Pro	Arg	Gly
		20					25					30			
Phe	Gln	Pro	Gln	Pro	Gly	Gly	Asn	Arg	Thr	Glu	Ser	Pro	Glu	Pro	Asn
	35					40					45				
Ala	Thr	Ala	Thr	Pro	Ala	Ile	Pro	Thr	Ile	Leu	Val	Thr	Ser	Val	Thr
50					55					60					
Ser	Glu	Thr	Pro	Ala	Thr	Ser	Ala	Pro	Glu	Ala	Glu	Gly	Pro	Gln	Ser
65				70					75					80	
Gly	Gly	Leu	Pro	Pro	Pro	Pro	Arg	Ala	Val	Pro	Ser	Ser	Ser	Ser	Pro
			85					90					95		
Gln	Ala	Gln	Ala	Leu	Thr	Glu	Asp	Gly	Arg	Pro	Cys	Arg	Phe	Pro	Phe
		100					105					110			
Arg	Tyr	Gly	Gly	Arg	Met	Leu	His	Ala	Cys	Thr	Ser	Glu	Gly	Ser	Ala
	115					120					125				
His	Arg	Lys	Trp	Cys	Ala	Thr	Thr	His	Asn	Tyr	Asp	Arg	Asp	Arg	Ala
130					135					140					
Trp	Gly	Tyr	Cys	Val	Glu	Ala	Thr	Pro	Pro	Pro	Gly	Gly	Pro	Ala	Ala
145				150					155					160	
Leu	Asp	Pro	Cys	Ala	Ser	Gly	Pro	Cys	Leu	Asn	Gly	Gly	Ser	Cys	Ser
			165					170					175		
Asn	Thr	Gln	Asp	Pro	Gln	Ser	Tyr	His	Cys	Ser	Cys	Pro	Arg	Ala	Phe
		180					185					190			
Thr	Gly	Lys	Asp	Cys	Gly	Thr	Glu	Lys	Cys	Phe	Asp	Glu	Thr	Arg	Tyr
	195					200					205				
Glu	Tyr	Leu	Glu	Gly	Gly	Asp	Arg	Trp	Ala	Arg	Val	Arg	Gln	Gly	His
210					215					220					
Val	Glu	Gln	Cys	Glu	Cys	Phe	Gly	Gly	Arg	Thr	Trp	Cys	Glu	Gly	Thr
225				230					235					240	
Arg	His	Thr	Ala	Cys	Leu	Ser	Ser	Pro	Cys	Leu	Asn	Gly	Gly	Thr	Cys
			245					250					255		
His	Leu	Ile	Val	Ala	Thr	Gly	Thr	Thr	Val	Cys	Ala	Cys	Pro	Pro	Gly
		260					265					270			
Phe	Ala	Gly	Arg	Leu	Cys	Asn	Ile	Glu	Pro	Asp	Glu	Arg	Cys	Phe	Leu
	275					280					285				
Gly	Asn	Gly	Thr	Gly	Tyr	Arg	Gly	Val	Ala	Ser	Thr	Ser	Ala	Ser	Gly
290					295					300					
Leu	Ser	Cys	Leu	Ala	Trp	Asn	Ser	Asp	Leu	Leu	Tyr	Gln	Glu	Leu	His
305				310					315					320	
Val	Asp	Ser	Val	Gly	Ala	Ala	Ala	Leu	Leu	Gly	Leu	Gly	Pro	His	Ala
			325					330					335		

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Tyr Cys Arg Asn Pro Asp Asn Asp Glu Arg Pro Trp Cys Tyr Val Val
            340                 345                 350
Lys Asp Ser Ala Leu Ser Trp Glu Tyr Cys Arg Leu Glu Ala Cys Glu
        355                 360                 365
Ser Leu Thr Arg Val Gln Leu Ser Pro Asp Leu Leu Ala Thr Leu Pro
    370                 375                 380
Glu Pro Ala Ser Pro Gly Arg Gln Ala Cys Gly Arg Arg His Lys Lys
385                 390                 395                 400
Arg Thr Phe Leu Arg Pro Arg Ile Ile Gly Gly Ser Ser Ser Leu Pro
                405                 410                 415
Gly Ser His Pro Trp Leu Ala Ala Ile Tyr Ile Gly Asp Ser Phe Cys
            420                 425                 430
Ala Gly Ser Leu Val His Thr Cys Trp Val Val Ser Ala Ala His Cys
        435                 440                 445
Phe Ser His Ser Pro Pro Arg Asp Ser Val Ser Val Val Leu Gly Gln
    450                 455                 460
His Phe Phe Asn Arg Thr Thr Asp Val Thr Gln Thr Phe Gly Ile Glu
465                 470                 475                 480
Lys Tyr Ile Pro Tyr Thr Leu Tyr Ser Val Phe Asn Pro Ser Asp His
                485                 490                 495
Asp Leu Val Leu Ile Arg Leu Lys Lys Lys Gly Asp Arg Cys Ala Thr
            500                 505                 510
Arg Ser Gln Phe Val Gln Pro Ile Cys Leu Pro Glu Pro Gly Ser Thr
        515                 520                 525
Phe Pro Ala Gly His Lys Cys Gln Ile Ala Gly Trp Gly His Leu Asp
    530                 535                 540
Glu Asn Val Ser Gly Tyr Ser Ser Ser Leu Arg Glu Ala Leu Val Pro
545                 550                 555                 560
Leu Val Ala Asp His Lys Cys Ser Ser Pro Glu Val Tyr Gly Ala Asp
                565                 570                 575
Ile Ser Pro Asn Met Leu Cys Ala Gly Tyr Phe Asp Cys Lys Ser Asp
            580                 585                 590
Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Ala Cys Glu Lys Asn Gly
        595                 600                 605
Val Ala Tyr Leu Tyr Gly Ile Ile Ser Trp Gly Asp Gly Cys Gly Arg
    610                 615                 620
Leu His Lys Pro Gly Val Tyr Thr Arg Val Ala Asn Tyr Val Asp Trp
625                 630                 635                 640
Ile Asn Asp Arg Ile Arg Pro Pro Arg Arg Leu Val Ala Pro Ser
                645                 650                 655
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<210> 217
<211> 2360
<212> DNA
<213> Homo sapiens

<400> 217

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gagagccctg ctggcgcgcc tgcttctctg cgtcctggtc gtgagcgact ccaaaggcag 180
caatgaactt catcaagttc catcgaactg tgactgtcta aatggaggaa catgtgtgtc 240
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gcaaacgtac catgcccaca gatctgatgc tcttcagctg ggcctgggga aacataatta 480
ctgcaggaac ccagacaacc ggaggcgacc ctggtgctat gtgcaggtgg gcctaaagcc 540
gcttgtccaa gagtgcatgg tgcatgactg cgcagatgga aaaaagccct cctctcctcc 600
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agaagaatta aaatttcagt gtggccaaaa gactctgagg ccccgcttta agattattgg 660
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<210> 218
<211> 431
<212> PRT
<213> Homo sapiens

<400> 218
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20 25 30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
35 40 45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
50 55 60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65 70 75 80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
85 90 95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
100 105 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
115 120 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
130 135 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145 150 155 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg

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                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
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Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
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<210> 219
<211> 2653
<212> DNA
<213> Homo sapiens

<400> 219

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tgaatttaag ggacgctgtg aagcaatcat ggatgcaatg aagagagggc tctgctgtgt 240
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<210> 220
<211> 562
<212> PRT
<213> Homo sapiens

<400> 220

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Ala	Val	Phe	Val	Ser	Pro	Ser	Gln	Glu	Ile	His	Ala	Arg	Phe	Arg	Arg
			20					25				30			
Gly	Ala	Arg	Ser	Tyr	Gln	Val	Ile	Cys	Arg	Asp	Glu	Lys	Thr	Gln	Met
		35					40					45			
Ile	Tyr	Gln	Gln	His	Gln	Ser	Trp	Leu	Arg	Pro	Val	Leu	Arg	Ser	Asn
	50					55					60				
Arg	Val	Glu	Tyr	Cys	Trp	Cys	Asn	Ser	Gly	Arg	Ala	Gln	Cys	His	Ser
65					70					75					80
Val	Pro	Val	Lys	Ser	Cys	Ser	Glu	Pro	Arg	Cys	Phe	Asn	Gly	Gly	Thr
				85					90					95	
Cys	Gln	Gln	Ala	Leu	Tyr	Phe	Ser	Asp	Phe	Val	Cys	Gln	Cys	Pro	Glu
			100					105					110		
Gly	Phe	Ala	Gly	Lys	Cys	Cys	Glu	Ile	Asp	Thr	Arg	Ala	Thr	Cys	Tyr
		115					120					125			
Glu	Asp	Gln	Gly	Ile	Ser	Tyr	Arg	Gly	Thr	Trp	Ser	Thr	Ala	Glu	Ser
	130					135					140				
Gly	Ala	Glu	Cys	Thr	Asn	Trp	Asn	Ser	Ser	Ala	Leu	Ala	Gln	Lys	Pro
145					150					155					160
Tyr	Ser	Gly	Arg	Arg	Pro	Asp	Ala	Ile	Arg	Leu	Gly	Leu	Gly	Asn	His
				165					170					175	
Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Arg	Asp	Ser	Lys	Pro	Trp	Cys	Tyr	Val

```
            180                 185                 190
Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys
        195                 200                 205
Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg
    210                 215                 220
Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn
225                 230                 235                 240
Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala
                245                 250                 255
Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly
            260                 265                 270
Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp
        275                 280                 285
Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr
    290                 295                 300
Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala
305                 310                 315                 320
Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro
                325                 330                 335
Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile
            340                 345                 350
Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu
        355                 360                 365
Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu
    370                 375                 380
Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp
385                 390                 395                 400
Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser
                405                 410                 415
Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro
            420                 425                 430
Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly
        435                 440                 445
Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys
    450                 455                 460
Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His
465                 470                 475                 480
Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr
                485                 490                 495
Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp
            500                 505                 510
Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val
        515                 520                 525
Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly
    530                 535                 540
Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met
545                 550                 555                 560
Arg Pro
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<210> 221
<211> 2160
<212> DNA
<213> Homo sapiens

<400> 221
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tgaatttaag ggacgctgtg aagcaatcat ggatgcaatg aagagagggc tctgctgtgt 240
gctgctgctg tgtggagcag tcttcgtttc gcccagccag gaaatccatg cccgattcag 300
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<210> 222
<211> 291
<212> PRT
<213> Homo sapiens

<400> 222

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            20                  25                  30
Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met
        35                  40                  45
Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn
    50                  55                  60
Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser
65                  70                  75                  80
Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr
                85                  90                  95
Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu
            100                 105                 110
Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr
```

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        115                 120                 125
Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser
    130                 135                 140
Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro
145                 150                 155                 160
Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His
                165                 170                 175
Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val
            180                 185                 190
Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys
        195                 200                 205
Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg
    210                 215                 220
Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn
225                 230                 235                 240
Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala
                245                 250                 255
Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Thr Gly Arg Ser
            260                 265                 270
Val Ser Ser Pro Ala Thr Ala Ser Met Arg Pro Cys Leu Leu Ser Ile
        275                 280                 285
Arg Ser Gly
    290
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<210> 223
<211> 2534
<212> DNA
<213> Homo sapiens

<400> 223

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tgaatttaag ggacgctgtg aagcaatcat ggatgcaatg aagagagggc tctgctgtgt 240
gctgctgctg tgtggagcag tcttcgtttc gcccagccag gaaatccatg cccgattcag 300
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gtgctgtgaa atagatacca gggccacgtg ctacgaggac cagggcatca gctacagggg 480
cacgtggagc acagcggaga gtggcgccga gtgcaccaac tggaacagca gcgcgttggc 540
ccagaagccc tacagcgggc ggaggccaga cgccatcagg ctgggcctgg ggaaccacaa 600
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atcacaacat ttacttaaca gaacagtcac cgacaacatg ctgtgtgctg gagacactcg 1560
gagcggcggg ccccaggcaa acttgcacga cgcctgccag ggcgattcgg gaggcccccc 1620
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<210> 224
<211> 516
<212> PRT
<213> Homo sapiens

<400> 224
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
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            20                  25                  30
Gly Ala Arg Ser Tyr Gln Gly Cys Ser Glu Pro Arg Cys Phe Asn Gly
        35                  40                  45
Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys
    50                  55                  60
Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr
65                  70                  75                  80
Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala
                85                  90                  95
Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln
            100                 105                 110
Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly
        115                 120                 125
Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys
    130                 135                 140
Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro
145                 150                 155                 160
Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala
                165                 170                 175
Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro
            180                 185                 190
Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro
        195                 200                 205
Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro
    210                 215                 220
Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu
225                 230                 235                 240
Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg
                245                 250                 255
Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp
            260                 265                 270
Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg
```

```
        275                 280                 285
Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys
    290                 295                 300
Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His
305                 310                 315                 320
His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu
                325                 330                 335
Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe
            340                 345                 350
Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser
        355                 360                 365
Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys
    370                 375                 380
Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu
385                 390                 395                 400
Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg
                405                 410                 415
Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser
            420                 425                 430
Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly
        435                 440                 445
Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln
    450                 455                 460
Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr
465                 470                 475                 480
Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val
                485                 490                 495
Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp
            500                 505                 510
Asn Met Arg Pro
        515
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<210> 225
<211> 2732
<212> DNA
<213> Homo sapiens

<400> 225

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gatgactatg tgaataccca gggggcttca ctgttcagtg tcactaagaa gcagctggga 180
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cctctggttt gcttcgagaa ggacaaatac attttacaag gagtcacttc ttggggtctt 2400
ggctgtgcac gccccaataa gcctggtgtc tatgttcgtg tttcaaggtt tgttacttgg 2460
attgagggag tgatgagaaa taattaattg gacgggagac agagtgacgc actgactcac 2520
ctagaggctg ggacgtgggt agggatttag catgctggaa ataactggca gtaatcaaac 2580
gaagacactg tccccagcta ccagctacgc caaacctcgg catttttgt gttattttct 2640
gactgctgga ttctgtagta aggtgacata gctatgacat ttgttaaaaa taaactctgt 2700
acttaacttt gatttgagta aattttggtt tt 2732

<210> 226
<211> 810
<212> PRT
<213> Homo sapiens

<400> 226

Met	Glu	His	Lys	Glu	Val	Val	Leu	Leu	Leu	Leu	Leu	Phe	Leu	Lys	Ser
1				5				10					15		
Gly	Gln	Gly	Glu	Pro	Leu	Asp	Asp	Tyr	Val	Asn	Thr	Gln	Gly	Ala	Ser
			20					25				30			
Leu	Phe	Ser	Val	Thr	Lys	Lys	Gln	Leu	Gly	Ala	Gly	Ser	Ile	Glu	Glu
		35					40					45			
Cys	Ala	Ala	Lys	Cys	Glu	Glu	Asp	Glu	Glu	Phe	Thr	Cys	Arg	Ala	Phe
	50					55					60				
Gln	Tyr	His	Ser	Lys	Glu	Gln	Gln	Cys	Val	Ile	Met	Ala	Glu	Asn	Arg
65					70					75					80
Lys	Ser	Ser	Ile	Ile	Ile	Arg	Met	Arg	Asp	Val	Val	Leu	Phe	Glu	Lys
				85					90					95	
Lys	Val	Tyr	Leu	Ser	Glu	Cys	Lys	Thr	Gly	Asn	Gly	Lys	Asn	Tyr	Arg
			100					105					110		
Gly	Thr	Met	Ser	Lys	Thr	Lys	Asn	Gly	Ile	Thr	Cys	Gln	Lys	Trp	Ser
		115					120					125			
Ser	Thr	Ser	Pro	His	Arg	Pro	Arg	Phe	Ser	Pro	Ala	Thr	His	Pro	Ser
	130					135					140				
Glu	Gly	Leu	Glu	Glu	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Asn	Asp	Pro	Gln
145					150					155					160
Gly	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro	Glu	Lys	Arg	Tyr	Asp	Tyr	Cys
				165					170					175	
Asp	Ile	Leu	Glu	Cys	Glu	Glu	Glu	Cys	Met	His	Cys	Ser	Gly	Glu	Asn
			180					185					190		

```
Tyr Asp Gly Lys Ile Ser Lys Thr Met Ser Gly Leu Glu Cys Gln Ala
        195                 200                 205
Trp Asp Ser Gln Ser Pro His Ala His Gly Tyr Ile Pro Ser Lys Phe
    210                 215                 220
Pro Asn Lys Asn Leu Lys Lys Asn Tyr Cys Arg Asn Pro Asp Arg Glu
225                 230                 235                 240
Leu Arg Pro Trp Cys Phe Thr Thr Asp Pro Asn Lys Arg Trp Glu Leu
                245                 250                 255
Cys Asp Ile Pro Arg Cys Thr Thr Pro Pro Pro Ser Ser Gly Pro Thr
            260                 265                 270
Tyr Gln Cys Leu Lys Gly Thr Gly Glu Asn Tyr Arg Gly Asn Val Ala
        275                 280                 285
Val Thr Val Ser Gly His Thr Cys Gln His Trp Ser Ala Gln Thr Pro
    290                 295                 300
His Thr His Asn Arg Thr Pro Glu Asn Phe Pro Cys Lys Asn Leu Asp
305                 310                 315                 320
Glu Asn Tyr Cys Arg Asn Pro Asp Gly Lys Arg Ala Pro Trp Cys His
                325                 330                 335
Thr Thr Asn Ser Gln Val Arg Trp Glu Tyr Cys Lys Ile Pro Ser Cys
            340                 345                 350
Asp Ser Ser Pro Val Ser Thr Glu Gln Leu Ala Pro Thr Ala Pro Pro
        355                 360                 365
Glu Leu Thr Pro Val Val Gln Asp Cys Tyr His Gly Asp Gly Gln Ser
    370                 375                 380
Tyr Arg Gly Thr Ser Ser Thr Thr Thr Thr Gly Lys Lys Cys Gln Ser
385                 390                 395                 400
Trp Ser Ser Met Thr Pro His Arg His Gln Lys Thr Pro Glu Asn Tyr
                405                 410                 415
Pro Asn Ala Gly Leu Thr Met Asn Tyr Cys Arg Asn Pro Asp Ala Asp
            420                 425                 430
Lys Gly Pro Trp Cys Phe Thr Thr Asp Pro Ser Val Arg Trp Glu Tyr
        435                 440                 445
Cys Asn Leu Lys Lys Cys Ser Gly Thr Glu Ala Ser Val Val Ala Pro
    450                 455                 460
Pro Pro Val Val Leu Leu Pro Asp Val Glu Thr Pro Ser Glu Glu Asp
465                 470                 475                 480
Cys Met Phe Gly Asn Gly Lys Gly Tyr Arg Gly Lys Arg Ala Thr Thr
                485                 490                 495
Val Thr Gly Thr Pro Cys Gln Asp Trp Ala Ala Gln Glu Pro His Arg
            500                 505                 510
His Ser Ile Phe Thr Pro Glu Thr Asn Pro Arg Ala Gly Leu Glu Lys
        515                 520                 525
Asn Tyr Cys Arg Asn Pro Asp Gly Asp Val Gly Gly Pro Trp Cys Tyr
    530                 535                 540
Thr Thr Asn Pro Arg Lys Leu Tyr Asp Tyr Cys Asp Val Pro Gln Cys
545                 550                 555                 560
Ala Ala Pro Ser Phe Asp Cys Gly Lys Pro Gln Val Glu Pro Lys Lys
                565                 570                 575
Cys Pro Gly Arg Val Val Gly Gly Cys Val Ala His Pro His Ser Trp
            580                 585                 590
Pro Trp Gln Val Ser Leu Arg Thr Arg Phe Gly Met His Phe Cys Gly
        595                 600                 605
Gly Thr Leu Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His Cys Leu
    610                 615                 620
Glu Lys Ser Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly Ala His
625                 630                 635                 640
Gln Glu Val Asn Leu Glu Pro His Val Gln Glu Ile Glu Val Ser Arg
                645                 650                 655
```

```
Leu Phe Leu Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys Leu Ser
            660                 665                 670
Ser Pro Ala Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu Pro Ser
        675                 680                 685
Pro Asn Tyr Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr Gly Trp
    690                 695                 700
Gly Glu Thr Gln Gly Thr Phe Gly Ala Gly Leu Leu Lys Glu Ala Gln
705                 710                 715                 720
Leu Pro Val Ile Glu Asn Lys Val Cys Asn Arg Tyr Glu Phe Leu Asn
                725                 730                 735
Gly Arg Val Gln Ser Thr Glu Leu Cys Ala Gly His Leu Ala Gly Gly
            740                 745                 750
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Phe Glu
        755                 760                 765
Lys Asp Lys Tyr Ile Leu Gln Gly Val Thr Ser Trp Gly Leu Gly Cys
    770                 775                 780
Ala Arg Pro Asn Lys Pro Gly Val Tyr Val Arg Val Ser Arg Phe Val
785                 790                 795                 800
Thr Trp Ile Glu Gly Val Met Arg Asn Asn
                805                 810
```

<210> 227
<211> 1527
<212> DNA
<213> Homo sapiens

<400> 227

```
ggcggacaaa gcccgattgt tcctgggccc tttccccatc gcgcctgggc ctgctcccca 60
gcccggggca ggggcggggg ccagtgtggt gacacacgct gtagctgtct ccccggctgg 120
ctggctcgct ctctcctggg gacacagagg tcggcaggca gcacacagag ggacctacgg 180
gcagctgttc cttcccccga ctcaagaatc cccggaggcc cggaggcctg cagcaggagc 240
ggccatgaag aagctgatgg tggtgctgag tctgattgct gcagcctggg cagaggagca 300
gaataagttg gtgcatggcg gaccctgcga caagacatct cacccctacc aagctgccct 360
ctacacctcg ggccacttgc tctgtggtgg ggtccttatc catccactgt gggtcctcac 420
agctgcccac tgcaaaaaac cgaatcttca ggtcttcctg gggaagcata accttcggca 480
aagggagagt tcccaggagc agagttctgt tgtccgggct gtgatccacc ctgactatga 540
tgccgccagc catgaccagg acatcatgct gttgcgcctg gcacgcccag ccaaactctc 600
tgaactcatc cagccccttc ccctggagag ggactgctca gccaacacca ccagctgcca 660
catcctgggc tggggcaaga cagcagatgg tgatttccct gacaccatcc agtgtgcata 720
catccacctg gtgtcccgtg aggagtgtga gcatgcctac cctggccaga tcacccagaa 780
catgttgtgt gctggggatg agaagtacgg gaaggattcc tgccagggtg attctggggg 840
tccgctggta tgtggagacc acctccgagg ccttgtgtca tggggtaaca tcccctgtgg 900
atcaaaggag aagccaggag tctacaccaa cgtctgcaga tacacgaact ggatccaaaa 960
aaccattcag gccaagtgac cctgacatgt gacatctacc tcccgaccta ccaccccact 1020
ggctggttcc agaacgtctc tcacctagac cttgcctccc ctcctctcct gcccagctct 1080
gaccctgatg cttaataaac gcagcgacgt gagggtcctg attctccctg gttttacccc 1140
agctccatcc ttgcatcact ggggaggacg tgatgagtga ggacttgggt cctcggtctt 1200
acccccacca ctaagagaat acaggaaaat cccttctagg catctcctct ccccaaccct 1260
tccacacgtt tgatttcttc ctgcagaggc ccagccacgt gtctggaatc ccagctccgc 1320
tgcttactgt cggtgtcccc ttgggatgta cctttcttca ctgcagattt ctcacctgta 1380
agatgaagat aaggatgata cagtctccat aaggcagtgg ctgttggaaa gatttaaggt 1440
ttcacaccta tgacatacat ggaatagcac ctgggccacc atgcactcaa taaagaatga 1500
attttattat gaaaaaaaaa aaaaaaa                                    1527
```

<210> 228
<211> 244
<212> PRT

<213> Homo sapiens

<400> 228

```
Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Ala Trp Ala
 1               5                  10                  15
Glu Glu Gln Asn Lys Leu Val His Gly Gly Pro Cys Asp Lys Thr Ser
            20                  25                  30
His Pro Tyr Gln Ala Ala Leu Tyr Thr Ser Gly His Leu Leu Cys Gly
        35                  40                  45
Gly Val Leu Ile His Pro Leu Trp Val Leu Thr Ala Ala His Cys Lys
    50                  55                  60
Lys Pro Asn Leu Gln Val Phe Leu Gly Lys His Asn Leu Arg Gln Arg
65                  70                  75                  80
Glu Ser Ser Gln Glu Gln Ser Ser Val Val Arg Ala Val Ile His Pro
                85                  90                  95
Asp Tyr Asp Ala Ala Ser His Asp Gln Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln Pro Leu Pro Leu Glu
        115                 120                 125
Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His Ile Leu Gly Trp Gly
    130                 135                 140
Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile Gln Cys Ala Tyr Ile
145                 150                 155                 160
His Leu Val Ser Arg Glu Glu Cys Glu His Ala Tyr Pro Gly Gln Ile
                165                 170                 175
Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys Tyr Gly Lys Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Asp His Leu Arg
        195                 200                 205
Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly Ser Lys Glu Lys Pro
    210                 215                 220
Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn Trp Ile Gln Lys Thr
225                 230                 235                 240
Ile Gln Ala Lys
```

<210> 229
<211> 1527
<212> DNA
<213> Homo sapiens

<400> 229

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aggacgttcc agaagcatct ggggacagaa ccagcctctt ccagggaggc ctgggagctg 60
ggggtgtgtg tctggcagtc cctgcagccc tgggctctgc ggcccctgcg tcctccgctt 120
ggctctgcca ctgcatctga gtgtcttctc tcctcacggc tccccgcatt tctaactctt 180
tctgcctcct cgtctcaaag ctgttccttc ccccgactca agaatccccg gaggcccgga 240
ggcctgcagc aggagcggcc atgaagaagc tgatggtggt gctgagtctg attgctgcag 300
cctgggcaga ggagcagaat aagttggtgc atggcggacc ctgcgacaag acatctcacc 360
cctaccaagc tgccctctac acctcgggcc acttgctctg tggtggggtc cttatccatc 420
cactgtgggt cctcacagct gcccactgca aaaaaccgaa tcttcaggtc ttcctgggga 480
agcataacct tcggcaaagg gagagttccc aggagcagag ttctgttgtc cgggctgtga 540
tccaccctga ctatgatgcc gccagccatg accaggacat catgctgttg cgcctggcac 600
gcccagccaa actctctgaa ctcatccagc cccttccccc ggagagggac tgctcagcca 660
acaccaccag ctgccacatc ctgggctggg gcaagacagc agatggtgat ttccctgaca 720
ccatccagtg tgcatacatc cacctggtgt cccgtgagga gtgtgagcat gcctaccctg 780
gccagatcac ccagaacatg ttgtgtgctg gggatgagaa gtacgggaag gattcctgcc 840
agggtgattc tgggggtccg ctggtatgtg gagaccacct ccgaggcctt gtgtcatggg 900
```

```
gtaacatccc ctgtggatca aaggagaagc caggagtcta caccaacgtc tgcagataca 960
cgaactggat ccaaaaaacc attcaggcca agtgaccctg acatgtgaca tctacctccc 1020
gacctaccac cccactggct ggttccagaa cgtctctcac ctagaccttg cctcccctcc 1080
tctcctgccc agctctgacc ctgatgctta ataaacgcag cgacgtgagg gtcctgattc 1140
tccctggttt taccccagct ccatccttgc atcactgggg aggacgtgat gagtgaggac 1200
ttgggtcctc ggtcttaccc ccaccactaa gagaatacag gaaaatccct tctaggcatc 1260
tcctctcccc aacccttcca cacgtttgat ttcttcctgc agaggcccag ccacgtgtct 1320
ggaatcccag ctccgctgct tactgtcggt gtcccttgg gatgtacctt tcttcactgc 1380
agatttctca cctgtaagat gaagataagg atgatacagt ctccataagg cagtggctgt 1440
tggaaagatt taaggtttca cacctatgac atacatggaa tagcacctgg gccaccatgc 1500
actcaataaa gaatgaattt tattatg                                     1527
```

<210> 230
<211> 244
<212> PRT
<213> Homo sapiens

<400> 230

```
Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Ala Trp Ala
 1               5                  10                  15
Glu Glu Gln Asn Lys Leu Val His Gly Gly Pro Cys Asp Lys Thr Ser
            20                  25                  30
His Pro Tyr Gln Ala Ala Leu Tyr Thr Ser Gly His Leu Leu Cys Gly
        35                  40                  45
Gly Val Leu Ile His Pro Leu Trp Val Leu Thr Ala Ala His Cys Lys
    50                  55                  60
Lys Pro Asn Leu Gln Val Phe Leu Gly Lys His Asn Leu Arg Gln Arg
65                  70                  75                  80
Glu Ser Ser Gln Glu Gln Ser Ser Val Val Arg Ala Val Ile His Pro
                85                  90                  95
Asp Tyr Asp Ala Ala Ser His Asp Gln Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln Pro Leu Pro Leu Glu
        115                 120                 125
Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His Ile Leu Gly Trp Gly
    130                 135                 140
Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile Gln Cys Ala Tyr Ile
145                 150                 155                 160
His Leu Val Ser Arg Glu Glu Cys Glu His Ala Tyr Pro Gly Gln Ile
                165                 170                 175
Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys Tyr Gly Lys Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Asp His Leu Arg
        195                 200                 205
Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly Ser Lys Glu Lys Pro
    210                 215                 220
Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn Trp Ile Gln Lys Thr
225                 230                 235                 240
Ile Gln Ala Lys
```

<210> 231
<211> 1495
<212> DNA
<213> Homo sapiens

<400> 231

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aggacgttcc agaagcatct ggggacagaa ccagcctctt ccagggaggc ctgggagctg 60
ggggtgtgtg tctggcagtc cctgcagccc tgggctctgc ggcccctgcg tcctccgctt 120
ggctctgcca ctgcatctga gtgtcttctc tcctcacggc tccccgcatt tctaactctt 180
tctgcctcct cgtctcaaag ctgttccttc ccccgactca agaatccccg gaggcccgga 240
ggcctgcagc agcctgggca gaggagcaga ataagttggt gcatggcgga ccctgcgaca 300
agacatctca cccctaccaa gctgccctct acacctcggg ccacttgctc tgtggtgggg 360
tccttatcca tccactgtgg gtcctcacag ctgcccactg caaaaaaccg aatcttcagg 420
tcttcctggg gaagcataac cttcggcaaa gggagagttc ccaggagcag agttctgttg 480
tccgggctgt gatccaccct gactatgatg ccgccagcca tgaccaggac atcatgctgt 540
tgcgcctggc acgcccagcc aaactctctg aactcatcca gccccttccc ctggagaggg 600
actgctcagc caacaccacc agctgccaca tcctgggctg gggcaagaca gcagatggtg 660
atttccctga caccatccag tgtgcataca tccacctggt gtcccgtgag gagtgtgagc 720
atgcctaccc tggccagatc acccagaaca tgttgtgtgc tggggatgag aagtacggga 780
aggattcctg ccagggtgat tctgggggtc cgctggtatg tggagaccac ctccgaggcc 840
ttgtgtcatg gggtaacatc ccctgtggat caaaggagaa gccaggagtc tacaccaacg 900
tctgcagata cacgaactgg atccaaaaaa ccattcaggc caagtgaccc tgacatgtga 960
catctacctc ccgacctacc accccactgg ctggttccag aacgtctctc acctagacct 1020
tgcctccccc cctctcctgc ccagctctga ccctgatgct taataaacgc agcgacgtga 1080
gggtcctgat tctccctggt tttaccccag ctccatcctt gcatcactgg ggaggacgtg 1140
atgagtgagg acttgggtcc tcggtcttac ccccaccact aagagaatac aggaaaatcc 1200
cttctaggca tctcctctcc ccaacccttc cacacgtttg atttcttcct gcagaggccc 1260
agccacgtgt ctggaatccc agctccgctg cttactgtcg gtgtcccctt gggatgtacc 1320
tttcttcact gcagatttct cacctgtaag atgaagataa ggatgataca gtctccataa 1380
ggcagtggct gttggaaaga tttaaggttt cacacctatg acatacatgg aatagcacct 1440
gggccaccat gcactcaata aagaatgaat tttattatga aaaaaaaaaa aaaaa      1495
```

<210> 232
<211> 137
<212> PRT
<213> Homo sapiens

<400> 232

```
Met Leu Leu Arg Leu Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln
 1               5                  10                  15
Pro Leu Pro Leu Glu Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His
            20                  25                  30
Ile Leu Gly Trp Gly Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile
        35                  40                  45
Gln Cys Ala Tyr Ile His Leu Val Ser Arg Glu Glu Cys Glu His Ala
    50                  55                  60
Tyr Pro Gly Gln Ile Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys
65                  70                  75                  80
Tyr Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
                85                  90                  95
Gly Asp His Leu Arg Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly
            100                 105                 110
Ser Lys Glu Lys Pro Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn
        115                 120                 125
Trp Ile Gln Lys Thr Ile Gln Ala Lys
    130                 135
```

<210> 233
<211> 1386
<212> DNA
<213> Homo sapiens

<400> 233

aggacgttcc agaagcatct ggggacagaa ccagcctctt ccagggaggc ctgggagctg 60
ggggtgtgtg tctggcagtc cctgcagccc tgggctctgc ggcccctgcg tcctccgctt 120
ggctctgcca ctgcatctga gtgtcttctc tcctcacggc tccccgcatt tctaactctt 180
tctgcctcct cgtctcaaag ctgttccttc ccccgactca agaatccccg gaggcccgga 240
ggcctgcagc aggagcggcc atgaagaagc tgatggtggt gctgagtctg attgctgcag 300
gaatcttcag gtcttcctgg ggaagcataa ccttcggcaa agggagagtt cccaggagca 360
gagttctgtt gtccgggctg tgatccaccc tgactatgat gccgccagcc atgaccagga 420
catcatgctg ttgcgcctgg cacgcccagc caaactctct gaactcatcc agccccttcc 480
cctggagagg gactgctcag ccaacaccac cagctgccac atcctgggct ggggcaagac 540
agcagatggt gatttccctg acaccatcca gtgtgcatac atccacctgg tgtcccgtga 600
ggagtgtgag catgcctacc ctggccagat cacccagaac atgttgtgtg ctggggatga 660
gaagtacggg aaggattcct gccagggtga ttctgggggt ccgctggtat gtggagacca 720
cctccgaggc cttgtgtcat ggggtaacat cccctgtgga tcaaaggaga agccaggagt 780
ctacaccaac gtctgcagat acacgaactg gatccaaaaa accattcagg ccaagtgacc 840
ctgacatgtg acatctacct cccgacctac caccccactg gctggttcca gaacgtctct 900
cacctagacc ttgcctcccc tcctctcctg cccagctctg accctgatgc ttaataaacg 960
cagcgacgtg agggtcctga ttctccctgg ttttacccca gctccatcct tgcatcactg 1020
gggaggacgt gatgagtgag gacttgggtc ctcggtctta cccccaccac taagagaata 1080
caggaaaatc ccttctaggc atctcctctc cccaaccctt ccacacgttt gatttcttcc 1140
tgcagaggcc cagccacgtg tctggaatcc cagctccgct gcttactgtc ggtgtcccct 1200
tgggatgtac ctttcttcac tgcagatttc tcacctgtaa gatgaagata aggatgatac 1260
agtctccata aggcagtggc tgttggaaag atttaaggtt tcacacctat gacatacatg 1320
gaatagcacc tgggccacca tgcactcaat aaagaatgaa ttttattatg aaaaaaaaaa 1380
aaaaaa 1386

<210> 234
<211> 40
<212> PRT
<213> Homo sapiens

<400> 234
Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Gly Ile Phe
 1   5   10   15
Arg Ser Ser Trp Gly Ser Ile Thr Phe Gly Lys Gly Arg Val Pro Arg
            20   25   30
Ser Arg Val Leu Leu Ser Gly Leu
        35   40

<210> 235
<211> 3351
<212> DNA
<213> Homo sapiens

<400> 235
gcccgagaag ctggggagca tggaccagac cccgcagcgc tggcaccatg acgctcgccc 60
gcttcgtgct agccctgatg ttaggggcgc tccccgaagt ggtcggcttt gattctgtcc 120
tcaatgattc cctccaccac agccaccgcc attcgccccc tgcgggtccg cactaccccc 180
attaccttcc cacccagcag cggcccccga cgacgcgtcc gccgccgcct ctcccgcgct 240
tcccgcgccc cccgcgggcg ctccctgccc agcgcccgca cgccctccag gccgggcaca 300
cgccccggcc gcacccctgg ggctgccccg ccggcgagcc atgggtcagc gtgacggact 360
tcggcgcccc gtgtctgcgg tgggcggagg tgccaccctt cctggagcgg tcgcccccag 420
cgagctgggc tcagctgcga ggacagcgcc acaacttttg tcggagcccc gacggcgcgg 480
gcagaccctg gtgtttctac ggagacgccc gtggcaaggt ggactggggc tactgcgact 540
gcagacacgg atcagtacga cttcgtggcg gcaaaaatga gtttgaaggc acagtggaag 600
tatatgcaag tggagtttgg ggcactgtct gtagcagcca ctgggatgat tctgatgcat 660
cagtcatttg tcaccagctg cagctgggag gaaaaggaat agcaaaacaa accccgtttt 720
ctggactggg ccttattccc atttattgga gcaatgtccg ttgccgagga gatgaagaaa 780

```
atatactgct ttgtgaaaaa gacatctggc agggtggggt gtgtcctcag aagatggcag 840
ctgctgtcac gtgtagcttt tcccatggcc caacgttccc catcattcgc cttgctggag 900
gcagcagtgt gcatgaaggc cgggtggagc tctaccatgc tggccagtgg ggaaccgttt 960
gtgatgacca atgggatgat gccgatgcag aagtgatctg caggcagctg ggcctcagtg 1020
gcattgccaa agcatggcat caggcatatt ttggggaagg gtctggccca gttatgttgg 1080
atgaagtacg ctgcactggg aatgagcttt caattgagca gtgtccaaag agctcctggg 1140
gagagcataa ctgtggccat aaagaagatg ctggagtgtc ctgtaccccc ctaacagatg 1200
gggtcatcag acttgcaggt gggaaaggca gccatgaggg tcgcttggag gtatattaca 1260
gaggccagtg gggaactgtc tgtgatgatg gctggactga gctgaataca tacgtggttt 1320
gtcgacagtt gggatttaaa tatggtaaac aagcatctgc caaccatttt gaagaaagca 1380
cagggcccat atggttggat gacgtcagct gctcaggaaa ggaaaccaga tttcttcagt 1440
gttccaggcg acagtgggga aggcatgact gcagccaccg cgaagatgtt agcattgcct 1500
gctaccctgg cggcgaggga cacaggctct ctctgggttt tcctgtcaga ctgatggatg 1560
gagaaaataa gaaagaagga cgagtggagg ttttttatcaa tggccagtgg ggaacaatct 1620
gtgatgatgg atggactgat aaggatgcag ctgtgatctg tcgtcagctt ggctacaagg 1680
gtcctgccag agcaagaacc atggcttact ttggagaagg aaaaggaccc atccatgtgg 1740
ataatgtgaa gtgcacagga aatgagaggt ccttggctga ctgtatcaag caagatattg 1800
gaagacacaa ctgccgccac agtgaagatg caggagttat ttgtgattat tttggcaaga 1860
aggcctcagg taacagtaat aaagagtccc tctcatctgt ttgtggcttg agattactgc 1920
accgtcggca gaagcggatc attggtggga aaaattcttt aaggggtggt tggccttggc 1980
aggtttccct ccggctgaag tcatcccatg gagatggcag gctcctctgc ggggctacgc 2040
tcctgagtag ctgctgggtc ctcacagcag cacactgttt caagaggtat ggcaacagca 2100
ctaggagcta tgctgttagg gttggagatt atcatactct ggtaccagag gagtttgagg 2160
aagaaattgg agttcaacag attgtgattc atcgggagta tcgacccgac cgcagtgatt 2220
atgacatagc cctggttaga ttacaaggac cagaagagca atgtgccaga ttcagcagcc 2280
atgttttgcc agcctgttta ccactctgga gagagaggcc acagaaaaca gcatccaact 2340
gttacataac aggatggggt gacacaggac gagcctattc aagaacacta caacaagcag 2400
ccattccctt acttcctaaa aggttttgtg aagaacgtta taagggtcgg tttacaggga 2460
gaatgctttg tgctggaaac ctccatgaac acaaacgcgt ggacagctgc cagggagaca 2520
gcggaggacc actcatgtgt gaacggcccg gagagagctg ggtggtgtat ggggtgacct 2580
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atttaaacaa atggaaaact ttgaaccccc actattagca ctcagcagag atgacaacaa 2760
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aacatttttct accctaattt cactggagtg acttattcta agcctcatct atcccctacc 2940
tatttctcaa aatcattcta tgctgatttt acaaaagatc atttttacat ttgaactgag 3000
aacccctttt aattgaatca gtggtgtctg aaatcatatt aaatacccac atttgacata 3060
aatgcggtac cctttactac actcatgagt ggcatattta tgcttaggtc ttttcaaaag 3120
acttgacaag aaatcttcat attctctgta gcctttgtca agtgaggaaa tcagtggtta 3180
aagaattcca ctataaactt ttaggcctga ataggagtag taaagcctca aggacatctg 3240
cctgtcacaa tatattctca aagtgatctg atatttggaa acaagtatcc ttgttgagta 3300
ccaagtgcta cagaaaccat aagataaaaa tactttctac ctacagcgtg c          3351
```

<210> 236
<211> 875
<212> PRT
<213> Homo sapiens

<400> 236

```
Met Thr Leu Ala Arg Phe Val Leu Ala Leu Met Leu Gly Ala Leu Pro
 1               5                  10                  15
Glu Val Val Gly Phe Asp Ser Val Leu Asn Asp Ser Leu His His Ser
            20                  25                  30
His Arg His Ser Pro Pro Ala Gly Pro His Tyr Pro Tyr Tyr Leu Pro
        35                  40                  45
Thr Gln Gln Arg Pro Pro Thr Thr Arg Pro Pro Pro Pro Leu Pro Arg
    50                  55                  60
```

```
Phe Pro Arg Pro Pro Arg Ala Leu Pro Ala Gln Arg Pro His Ala Leu
65                  70                  75                  80
Gln Ala Gly His Thr Pro Arg Pro His Pro Trp Gly Cys Pro Ala Gly
                85                  90                  95
Glu Pro Trp Val Ser Val Thr Asp Phe Gly Ala Pro Cys Leu Arg Trp
            100                 105                 110
Ala Glu Val Pro Pro Phe Leu Glu Arg Ser Pro Pro Ala Ser Trp Ala
        115                 120                 125
Gln Leu Arg Gly Gln Arg His Asn Phe Cys Arg Ser Pro Asp Gly Ala
    130                 135                 140
Gly Arg Pro Trp Cys Phe Tyr Gly Asp Ala Arg Gly Lys Val Asp Trp
145                 150                 155                 160
Gly Tyr Cys Asp Cys Arg His Gly Ser Val Arg Leu Arg Gly Gly Lys
                165                 170                 175
Asn Glu Phe Glu Gly Thr Val Glu Val Tyr Ala Ser Gly Val Trp Gly
            180                 185                 190
Thr Val Cys Ser Ser His Trp Asp Asp Ser Asp Ala Ser Val Ile Cys
        195                 200                 205
His Gln Leu Gln Leu Gly Gly Lys Gly Ile Ala Lys Gln Thr Pro Phe
    210                 215                 220
Ser Gly Leu Gly Leu Ile Pro Ile Tyr Trp Ser Asn Val Arg Cys Arg
225                 230                 235                 240
Gly Asp Glu Glu Asn Ile Leu Leu Cys Glu Lys Asp Ile Trp Gln Gly
                245                 250                 255
Gly Val Cys Pro Gln Lys Met Ala Ala Ala Val Thr Cys Ser Phe Ser
            260                 265                 270
His Gly Pro Thr Phe Pro Ile Ile Arg Leu Ala Gly Gly Ser Ser Val
        275                 280                 285
His Glu Gly Arg Val Glu Leu Tyr His Ala Gly Gln Trp Gly Thr Val
    290                 295                 300
Cys Asp Asp Gln Trp Asp Asp Ala Asp Ala Glu Val Ile Cys Arg Gln
305                 310                 315                 320
Leu Gly Leu Ser Gly Ile Ala Lys Ala Trp His Gln Ala Tyr Phe Gly
                325                 330                 335
Glu Gly Ser Gly Pro Val Met Leu Asp Glu Val Arg Cys Thr Gly Asn
            340                 345                 350
Glu Leu Ser Ile Glu Gln Cys Pro Lys Ser Ser Trp Gly Glu His Asn
        355                 360                 365
Cys Gly His Lys Glu Asp Ala Gly Val Ser Cys Thr Pro Leu Thr Asp
    370                 375                 380
Gly Val Ile Arg Leu Ala Gly Gly Lys Gly Ser His Glu Gly Arg Leu
385                 390                 395                 400
Glu Val Tyr Tyr Arg Gly Gln Trp Gly Thr Val Cys Asp Asp Gly Trp
                405                 410                 415
Thr Glu Leu Asn Thr Tyr Val Val Cys Arg Gln Leu Gly Phe Lys Tyr
            420                 425                 430
Gly Lys Gln Ala Ser Ala Asn His Phe Glu Glu Ser Thr Gly Pro Ile
        435                 440                 445
Trp Leu Asp Asp Val Ser Cys Ser Gly Lys Glu Thr Arg Phe Leu Gln
    450                 455                 460
Cys Ser Arg Arg Gln Trp Gly Arg His Asp Cys Ser His Arg Glu Asp
465                 470                 475                 480
Val Ser Ile Ala Cys Tyr Pro Gly Gly Glu Gly His Arg Leu Ser Leu
                485                 490                 495
Gly Phe Pro Val Arg Leu Met Asp Gly Glu Asn Lys Lys Glu Gly Arg
            500                 505                 510
Val Glu Val Phe Ile Asn Gly Gln Trp Gly Thr Ile Cys Asp Asp Gly
        515                 520                 525
```

```
Trp Thr Asp Lys Asp Ala Ala Val Ile Cys Arg Gln Leu Gly Tyr Lys
    530                 535                 540
Gly Pro Ala Arg Ala Arg Thr Met Ala Tyr Phe Gly Glu Gly Lys Gly
545                 550                 555                 560
Pro Ile His Val Asp Asn Val Lys Cys Thr Gly Asn Glu Arg Ser Leu
                565                 570                 575
Ala Asp Cys Ile Lys Gln Asp Ile Gly Arg His Asn Cys Arg His Ser
            580                 585                 590
Glu Asp Ala Gly Val Ile Cys Asp Tyr Phe Gly Lys Lys Ala Ser Gly
        595                 600                 605
Asn Ser Asn Lys Glu Ser Leu Ser Ser Val Cys Gly Leu Arg Leu Leu
    610                 615                 620
His Arg Arg Gln Lys Arg Ile Ile Gly Gly Lys Asn Ser Leu Arg Gly
625                 630                 635                 640
Gly Trp Pro Trp Gln Val Ser Leu Arg Leu Lys Ser Ser His Gly Asp
                645                 650                 655
Gly Arg Leu Leu Cys Gly Ala Thr Leu Leu Ser Ser Cys Trp Val Leu
            660                 665                 670
Thr Ala Ala His Cys Phe Lys Arg Tyr Gly Asn Ser Thr Arg Ser Tyr
        675                 680                 685
Ala Val Arg Val Gly Asp Tyr His Thr Leu Val Pro Glu Glu Phe Glu
    690                 695                 700
Glu Glu Ile Gly Val Gln Gln Ile Val Ile His Arg Glu Tyr Arg Pro
705                 710                 715                 720
Asp Arg Ser Asp Tyr Asp Ile Ala Leu Val Arg Leu Gln Gly Pro Glu
                725                 730                 735
Glu Gln Cys Ala Arg Phe Ser Ser His Val Leu Pro Ala Cys Leu Pro
            740                 745                 750
Leu Trp Arg Glu Arg Pro Gln Lys Thr Ala Ser Asn Cys Tyr Ile Thr
        755                 760                 765
Gly Trp Gly Asp Thr Gly Arg Ala Tyr Ser Arg Thr Leu Gln Gln Ala
    770                 775                 780
Ala Ile Pro Leu Leu Pro Lys Arg Phe Cys Glu Glu Arg Tyr Lys Gly
785                 790                 795                 800
Arg Phe Thr Gly Arg Met Leu Cys Ala Gly Asn Leu His Glu His Lys
                805                 810                 815
Arg Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Met Cys Glu
            820                 825                 830
Arg Pro Gly Glu Ser Trp Val Val Tyr Gly Val Thr Ser Trp Gly Tyr
        835                 840                 845
Gly Cys Gly Val Lys Asp Ser Pro Gly Val Tyr Thr Lys Val Ser Ala
    850                 855                 860
Phe Val Pro Trp Ile Lys Ser Val Thr Lys Leu
865                 870                 875
```

<210> 237
<211> 1165
<212> DNA
<213> Homo sapiens

<400> 237
agaaggaaca gggagcggcc aggatgctga atctgctgct gctggcgctg cccgtcctgg 60
cgagccgcgc ctacgcggcc cctgccccag gccaggccct gcagcgagtg ggcatcgttg 120
ggggtcagga ggcccccagg agcaagtggc cctggcaggt gagcctgaga gtccgcgacc 180
gatactggat gcacttctgc gggggctccc tcatccaccc ccagtgggtg ctgaccgcag 240
cgcactgcgt gggaccggac gtcaaggatc tggccgccct cagggtgcaa ctgcgggagc 300
agcacctcta ctaccaggac cagctgctgc cggtcagcag gatcatcgtg cacccacagt 360

```
tctacaccgc ccagatcgga gcggacatcg ccctgctgga gctggaggag ccggtgaacg 420
tctccagcca cgtccacacg gtcaccctgc cccctgcctc agagaccttc ccccgggga 480
tgccgtgctg ggtcactggc tggggcgatg tggacaatga tgagcgcctc ccaccgccat 540
ttcctctgaa gcaggtgaag gtccccataa tggaaaacca catttgtgac gcaaaatacc 600
accttggcgc ctacacggga gacgacgtcc gcatcgtccg tgacgacatg ctgtgtgccg 660
ggaacacccg gagggactca tgccagggcg actccggagg gccctggtg tgcaaggtga 720
atggcacctg gctgcaggcg ggcgtggtca gctggggcga gggctgtgcc cagcccaacc 780
ggcctggcat ctacacccgt gtcacctact acttggactg gatccaccac tatgtcccca 840
aaaagccgtg agtcaggcct ggggtgtcca cctgggtcac tggagagcca gcccctcctg 900
tccaaaacac cactgcttcc tacccaggtg gcgactgccc cccacacctt ccctgccccg 960
tcctgagtgc cccttcctgt cctaagcccc ctgctctctt ctgagcccct tcccctgtcc 1020
tgaggaccct tcccatcct gagccccctt ccctgtccta agcctgacgc ctgcaccggg 1080
ccctccggcc ctcccctgcc caggcagctg gtggtgggcg ctaatcctcc tgagtgctgg 1140
acctcattaa agtgcatgga aatca                                      1165

<210> 238
<211> 275
<212> PRT
<213> Homo sapiens

<400> 238
Met Leu Asn Leu Leu Leu Leu Ala Leu Pro Val Leu Ala Ser Arg Ala
 1               5                  10                  15
Tyr Ala Ala Pro Ala Pro Gly Gln Ala Leu Gln Arg Val Gly Ile Val
            20                  25                  30
Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val Ser Leu
        35                  40                  45
Arg Val Arg Asp Arg Tyr Trp Met His Phe Cys Gly Gly Ser Leu Ile
    50                  55                  60
His Pro Gln Trp Val Leu Thr Ala Ala His Cys Val Gly Pro Asp Val
65                  70                  75                  80
Lys Asp Leu Ala Ala Leu Arg Val Gln Leu Arg Glu Gln His Leu Tyr
                85                  90                  95
Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His Pro Gln
            100                 105                 110
Phe Tyr Thr Ala Gln Ile Gly Ala Asp Ile Ala Leu Leu Glu Leu Glu
        115                 120                 125
Glu Pro Val Asn Val Ser Ser His Val His Thr Val Thr Leu Pro Pro
    130                 135                 140
Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr Gly Trp
145                 150                 155                 160
Gly Asp Val Asp Asn Asp Glu Arg Leu Pro Pro Pro Phe Pro Leu Lys
                165                 170                 175
Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala Lys Tyr
            180                 185                 190
His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Val Arg Asp Asp
        195                 200                 205
Met Leu Cys Ala Gly Asn Thr Arg Arg Asp Ser Cys Gln Gly Asp Ser
    210                 215                 220
Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln Ala Gly
225                 230                 235                 240
Val Val Ser Trp Gly Glu Gly Cys Ala Gln Pro Asn Arg Pro Gly Ile
                245                 250                 255
Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr Val Pro
            260                 265                 270
Lys Lys Pro
        275
```

<210> 239
<211> 1013
<212> DNA
<213> Homo sapiens

<400> 239
gttcccagaa gctccccagg ctctagtgca ggaggagaag gaggaggagc aggaggtgga 60
gattcccagt taaaaggctc cagaatcgtg taccaggcag agaactgaag tactggggcc 120
tcctccactg ggtccgaatc agtaggtgac cccgcccctg gattctggaa gacctcacca 180
tgggacgccc ccgacctcgt gcggccaaga cgtggatgtt cctgctcttg ctggggggag 240
cctgggcagg acactccagg gcacaggagg acaaggtgct ggggggtcat gagtgccaac 300
cccattcgca gccttggcag gcggccttgt tccagggcca gcaactactc tgtggcggtg 360
tccttgtagg tggcaactgg gtccttacag ctgcccactg taaaaaaccg aaatacacag 420
tacgcctggg agaccacagc ctacagaata aagatggccc agagcaagaa atacctgtgg 480
ttcagtccat cccacacccc tgctacaaca gcagcgatgt ggaggaccac aaccatgatc 540
tgatgcttct tcaactgcgt gaccaggcat ccctggggtc caaagtgaag cccatcagcc 600
tggcagatca ttgcacccag cctggccaga agtgcaccgt ctcaggctgg ggcactgtca 660
ccagtccccg agagaatttt cctgacactc tcaactgtgc agaagtaaaa atctttcccc 720
agaagaagtg tgaggatgct tacccggggc agatcacaga tggcatggtc tgtgcaggca 780
gcagcaaagg ggctgacacg tgccagggcg attctggagg ccccctggtg tgtgatggtg 840
cactccaggg catcacatcc tggggctcag acccctgtgg gaggtccgac aaacctggcg 900
tctataccaa catctgccgc tacctggact ggatcaagaa gatcataggc agcaagggct 960
gattctagga taagcactag atctccctta ataaactcac aactctctgg ttc 1013

<210> 240
<211> 260
<212> PRT
<213> Homo sapiens

<400> 240
Met Gly Arg Pro Arg Pro Arg Ala Ala Lys Thr Trp Met Phe Leu Leu
 1   5   10   15
Leu Leu Gly Gly Ala Trp Ala Gly His Ser Arg Ala Gln Glu Asp Lys
            20   25   30
Val Leu Gly Gly His Glu Cys Gln Pro His Ser Gln Pro Trp Gln Ala
        35   40   45
Ala Leu Phe Gln Gly Gln Gln Leu Leu Cys Gly Gly Val Leu Val Gly
    50   55   60
Gly Asn Trp Val Leu Thr Ala Ala His Cys Lys Lys Pro Lys Tyr Thr
65   70   75   80
Val Arg Leu Gly Asp His Ser Leu Gln Asn Lys Asp Gly Pro Glu Gln
                85   90   95
Glu Ile Pro Val Val Gln Ser Ile Pro His Pro Cys Tyr Asn Ser Ser
            100   105   110
Asp Val Glu Asp His Asn His Asp Leu Met Leu Leu Gln Leu Arg Asp
        115   120   125
Gln Ala Ser Leu Gly Ser Lys Val Lys Pro Ile Ser Leu Ala Asp His
    130   135   140
Cys Thr Gln Pro Gly Gln Lys Cys Thr Val Ser Gly Trp Gly Thr Val
145   150   155   160
Thr Ser Pro Arg Glu Asn Phe Pro Asp Thr Leu Asn Cys Ala Glu Val
                165   170   175
Lys Ile Phe Pro Gln Lys Lys Cys Glu Asp Ala Tyr Pro Gly Gln Ile
            180   185   190
Thr Asp Gly Met Val Cys Ala Gly Ser Ser Lys Gly Ala Asp Thr Cys
        195   200   205
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Asp Gly Ala Leu Gln Gly

```
    210                 215                 220
Ile Thr Ser Trp Gly Ser Asp Pro Cys Gly Arg Ser Asp Lys Pro Gly
225                 230                 235                 240
Val Tyr Thr Asn Ile Cys Arg Tyr Leu Asp Trp Ile Lys Lys Ile Ile
                245                 250                 255
Gly Ser Lys Gly
            260
```

<210> 241
<211> 1148
<212> DNA
<213> Homo sapiens

<400> 241
gttcccagaa gctccccagg ctctagtgca ggaggagaag gaggaggagc aggaggtgga 60
gattcccagt taaaaggctc cagaatcgtg taccaggcag agaactgaag tactggggcc 120
tcctccactg ggtccgaatc agtaggtgac cccgcccctg gattctggaa gacctcacca 180
tgggacgccc ccgacctcgt gcggccaaga cgtggatgtt cctgctcttg ctgggggggag 240
cctgggcagc gtgtggaagc ctggacctcc tcactaagtt gtatgcggag aacttgccgt 300
gtgtccattt gaacccacag tggccttccc agccctcgca ctgccccaga gggtggcgat 360
ccaaccctct ccctcctgct gcaggacact ccagggcaca ggaggacaag gtgctggggg 420
gtcatgagtg ccaaccccat tcgcagcctt ggcaggcggc cttgttccag ggccagcaac 480
tactctgtgg cggtgtcctt gtaggtggca actgggtcct tacagctgcc cactgtaaaa 540
aaccgaaata cacagtacgc ctgggagacc acagcctaca gaataaagat ggcccagagc 600
aagaaatacc tgtggttcag tccatcccac acccctgcta caacagcagc gatgtggagg 660
accacaacca tgatctgatg cttcttcaac tgcgtgacca ggcatccctg gggtccaaag 720
tgaagcccat cagcctggca gatcattgca cccagcctgg ccagaagtgc accgtctcag 780
gctggggcac tgtcaccagt ccccgagaga attttcctga cactctcaac tgtgcagaag 840
taaaaatctt tccccagaag aagtgtgagg atgcttaccc ggggcagatc acagatggca 900
tggtctgtgc aggcagcagc aaaggggctg acacgtgcca gggcgattct ggaggccccc 960
tggtgtgtga tggtgcactc cagggcatca catcctgggg ctcagacccc tgtgggaggt 1020
ccgacaaacc tggcgtctat accaacatct gccgctacct ggactggatc aagaagatca 1080
taggcagcaa gggctgattc taggataagc actagatctc ccttaataaa ctcacaactc 1140
tctggttc   1148

<210> 242
<211> 305
<212> PRT
<213> Homo sapiens

<400> 242
```
Met Gly Arg Pro Arg Pro Arg Ala Ala Lys Thr Trp Met Phe Leu Leu
 1               5                  10                  15
Leu Leu Gly Gly Ala Trp Ala Ala Cys Gly Ser Leu Asp Leu Leu Thr
            20                  25                  30
Lys Leu Tyr Ala Glu Asn Leu Pro Cys Val His Leu Asn Pro Gln Trp
        35                  40                  45
Pro Ser Gln Pro Ser His Cys Pro Arg Gly Trp Arg Ser Asn Pro Leu
    50                  55                  60
Pro Pro Ala Ala Gly His Ser Arg Ala Gln Glu Asp Lys Val Leu Gly
65                  70                  75                  80
Gly His Glu Cys Gln Pro His Ser Gln Pro Trp Gln Ala Ala Leu Phe
                85                  90                  95
Gln Gly Gln Gln Leu Leu Cys Gly Gly Val Leu Val Gly Gly Asn Trp
            100                 105                 110
Val Leu Thr Ala Ala His Cys Lys Lys Pro Lys Tyr Thr Val Arg Leu
        115                 120                 125
```

```
Gly Asp His Ser Leu Gln Asn Lys Asp Gly Pro Glu Gln Glu Ile Pro
    130                 135                 140
Val Val Gln Ser Ile Pro His Pro Cys Tyr Asn Ser Ser Asp Val Glu
145                 150                 155                 160
Asp His Asn His Asp Leu Met Leu Leu Gln Leu Arg Asp Gln Ala Ser
                165                 170                 175
Leu Gly Ser Lys Val Lys Pro Ile Ser Leu Ala Asp His Cys Thr Gln
            180                 185                 190
Pro Gly Gln Lys Cys Thr Val Ser Gly Trp Gly Thr Val Thr Ser Pro
        195                 200                 205
Arg Glu Asn Phe Pro Asp Thr Leu Asn Cys Ala Glu Val Lys Ile Phe
    210                 215                 220
Pro Gln Lys Lys Cys Glu Asp Ala Tyr Pro Gly Gln Ile Thr Asp Gly
225                 230                 235                 240
Met Val Cys Ala Gly Ser Ser Lys Gly Ala Asp Thr Cys Gln Gly Asp
                245                 250                 255
Ser Gly Gly Pro Leu Val Cys Asp Gly Ala Leu Gln Gly Ile Thr Ser
            260                 265                 270
Trp Gly Ser Asp Pro Cys Gly Arg Ser Asp Lys Pro Gly Val Tyr Thr
        275                 280                 285
Asn Ile Cys Arg Tyr Leu Asp Trp Ile Lys Lys Ile Ile Gly Ser Lys
    290                 295                 300
Gly
305
```

<210> 243
<211> 590
<212> DNA
<213> Homo sapiens

<400> 243
gttcccagaa gctccccagg ctctagtgca ggaggagaag gaggaggagc aggaggtgga 60
gattcccagt taaaaggctc cagaatcgtg taccaggcag agaactgaag tactggggcc 120
tcctccactg ggtccgaatc agtaggtgac cccgcccctg gattctggaa gacctcacca 180
tgggacgccc ccgacctcgt gcggccaaga cgtggatgtt cctgctcttg ctgggggggag 240
cctgggcaga gaatttttcct gacactctca actgtgcaga agtaaaaatc tttccccaga 300
agaagtgtga ggatgcttac ccggggcaga tcacagatgg catggtctgt gcaggcagca 360
gcaaaggggc tgacacgtgc cagggcgatt ctggaggccc cctggtgtgt gatggtgcac 420
tccagggcat cacatcctgg ggctcagacc cctgtgggag gtccgacaaa cctggcgtct 480
ataccaacat ctgccgctac ctggactgga tcaagaagat cataggcagc aagggctgat 540
tctaggataa gcactagatc tcccttaata aactcacaac tctctggttc 590

<210> 244
<211> 119
<212> PRT
<213> Homo sapiens

<400> 244
```
Met Gly Arg Pro Arg Pro Arg Ala Ala Lys Thr Trp Met Phe Leu Leu
 1               5                  10                  15
Leu Leu Gly Gly Ala Trp Ala Glu Asn Phe Pro Asp Thr Leu Asn Cys
            20                  25                  30
Ala Glu Val Lys Ile Phe Pro Gln Lys Lys Cys Glu Asp Ala Tyr Pro
        35                  40                  45
Gly Gln Ile Thr Asp Gly Met Val Cys Ala Gly Ser Ser Lys Gly Ala
    50                  55                  60
Asp Thr Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Asp Gly Ala
```

```
65                  70                  75                  80
Leu Gln Gly Ile Thr Ser Trp Gly Ser Asp Pro Cys Gly Arg Ser Asp
                85                  90                  95
Lys Pro Gly Val Tyr Thr Asn Ile Cys Arg Tyr Leu Asp Trp Ile Lys
            100                 105                 110
Lys Ile Ile Gly Ser Lys Gly
        115
```

<210> 245
<211> 456
<212> DNA
<213> Homo sapiens

<400> 245
gttcccagaa gctccccagg ctctagtgca ggaggagaag gaggaggagc aggaggtgga 60
gattcccagt taaaaggctc cagaatcgtg taccaggcag agaactgaag tactggggcc 120
tcctccactg ggtccgaatc agtaggtgac cccgcccctg gattctggaa gacctcacca 180
tgggacgccc ccgacctcgt gcggccaaga cgtggatgtt cctgctcttg ctggggggag 240
cctgggcagg gcgattctgg aggcccccctg gtgtgtgatg gtgcactcca gggcatcaca 300
tcctggggct cagacccctg tgggaggtcc gacaaacctg gcgtctatac caacatctgc 360
cgctacctgg actggatcaa gaagatcata ggcagcaagg gctgattcta ggataagcac 420
tagatctccc ttaataaact cacaactctc tggttc 456

<210> 246
<211> 32
<212> PRT
<213> Homo sapiens

<400> 246
```
Met Gly Arg Pro Arg Pro Arg Ala Ala Lys Thr Trp Met Phe Leu Leu
 1               5                  10                  15
Leu Leu Gly Gly Ala Trp Ala Gly Arg Phe Trp Arg Pro Pro Gly Val
            20                  25                  30
```

<210> 247
<211> 1580
<212> DNA
<213> Homo sapiens

<400> 247
catcctgcca cccctagcct tgctggggac gtgaaccctc tccccgcgcc tgggaagcct 60
tcttggcacc gggacccgga gaatccccac ggaagccagt tccaaaaggg atgaaaaggg 120
ggcgtttcgg gcactgggag aagcctgtat tccagggccc ctcccagagc aggaatctgg 180
gacccaggag tgccagcctc acccacgcag atcctggcca tgagagctcc gcacctccac 240
ctctccgccg cctctggcgc ccgggctctg gcgaagctgc tgccgctgct gatggcgcaa 300
ctctgggccg cagaggcggc gctgctcccc caaaacgaca cgcgcttgga ccccgaagcc 360
tatggctccc cgtgcgcgcg cggctcgcag ccctggcagg tctcgctctt caacggcctc 420
tcgttccact gcgcgggtgt cctggtggac cagagttggg tgctgacggc cgcgcactgc 480
ggaaacaagc cactgtgggc tcgagtaggg gatgaccacc tgctgcttct tcagggagag 540
cagctccgcc ggaccactcg ctctgttgtc catcccaagt accaccaggg ctcaggcccc 600
atcctgccaa ggcgaacgga tgagcacgat ctcatgttgc tgaagctggc caggcccgta 660
gtgctggggc cccgcgtccg ggccctgcag cttccctacc gctgtgctca gcccggagac 720
cagtgccagg ttgctggctg gggcaccacg gccgcccgga gagtgaagta caacaagggc 780
ctgacctgct ccagcatcac tatcctgagc cctaaagagt gtgaggtctt ctaccctggc 840
gtggtcacca acaacatgat atgtgctgga ctggaccggg gccaggaccc ttgccagagt 900
gactctggag gccccctggt ctgtgacgag accctccaag gcatcctctc gtggggtgtt 960

```
tacccctgtg gctctgccca gcatccagct gtctacaccc agatctgcaa atacatgtcc 1020
tggatcaata aagtcatacg ctccaactga tccagatgct acgctccagc tgatccagat 1080
gttatgctcc tgctgatcca gatgcccaga ggctccatcg tccatcctct tcctccccag 1140
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acatctcccc tctcacctca ttcccccacc tatccccatt ctctgcctgt actgaagctg 1260
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gtgactttgg gcaagccaag tgccctctct gaacctcagt ttcctcatct gcaaaatggg 1440
aacaatgacg tgcctacctc ttagacatgt tgtgaggaga ctatgatata acatgtgtat 1500
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aaggttacct gttgtcgtga                                            1580
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<210> 248
<211> 276
<212> PRT
<213> Homo sapiens

<400> 248

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Met Arg Ala Pro His Leu His Leu Ser Ala Ala Ser Gly Ala Arg Ala
 1               5                  10                  15
Leu Ala Lys Leu Leu Pro Leu Leu Met Ala Gln Leu Trp Ala Ala Glu
            20                  25                  30
Ala Ala Leu Leu Pro Gln Asn Asp Thr Arg Leu Asp Pro Glu Ala Tyr
        35                  40                  45
Gly Ser Pro Cys Ala Arg Gly Ser Gln Pro Trp Gln Val Ser Leu Phe
    50                  55                  60
Asn Gly Leu Ser Phe His Cys Ala Gly Val Leu Val Asp Gln Ser Trp
65                  70                  75                  80
Val Leu Thr Ala Ala His Cys Gly Asn Lys Pro Leu Trp Ala Arg Val
                85                  90                  95
Gly Asp Asp His Leu Leu Leu Leu Gln Gly Glu Gln Leu Arg Arg Thr
            100                 105                 110
Thr Arg Ser Val Val His Pro Lys Tyr His Gln Gly Ser Gly Pro Ile
        115                 120                 125
Leu Pro Arg Arg Thr Asp Glu His Asp Leu Met Leu Leu Lys Leu Ala
    130                 135                 140
Arg Pro Val Val Leu Gly Pro Arg Val Arg Ala Leu Gln Leu Pro Tyr
145                 150                 155                 160
Arg Cys Ala Gln Pro Gly Asp Gln Cys Gln Val Ala Gly Trp Gly Thr
                165                 170                 175
Thr Ala Ala Arg Arg Val Lys Tyr Asn Lys Gly Leu Thr Cys Ser Ser
            180                 185                 190
Ile Thr Ile Leu Ser Pro Lys Glu Cys Glu Val Phe Tyr Pro Gly Val
        195                 200                 205
Val Thr Asn Asn Met Ile Cys Ala Gly Leu Asp Arg Gly Gln Asp Pro
    210                 215                 220
Cys Gln Ser Asp Ser Gly Gly Pro Leu Val Cys Asp Glu Thr Leu Gln
225                 230                 235                 240
Gly Ile Leu Ser Trp Gly Val Tyr Pro Cys Gly Ser Ala Gln His Pro
                245                 250                 255
Ala Val Tyr Thr Gln Ile Cys Lys Tyr Met Ser Trp Ile Asn Lys Val
            260                 265                 270
Ile Arg Ser Asn
        275
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<210> 249
<211> 1443

<212> DNA
<213> Homo sapiens

<400> 249
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cgcccgggct ctggcgaagc tgctgccgct gctgatggcg caactctggg ccgcagaggc 180
ggcgctgctc ccccaaaacg acacgcgctt ggacccccgaa gcctatggct ccccgtgcgc 240
gcgcggctcg cagccctggc aggtctcgct cttcaacggc ctctcgttcc actgcgcggg 300
tgtcctggtg gaccagagtt gggtgctgac ggccgcgcac tgcggaaaca agccactgtg 360
ggctcgagta ggggatgacc acctgctgct tcttcaggga gagcagctcc gccggaccac 420
tcgctctgtt gtccatccca agtaccacca gggctcaggc cccatcctgc caaggcgaac 480
ggatgagcac gatctcatgt tgctgaagct ggccaggccc gtagtgctgg ggccccgcgt 540
ccgggccctg cagcttccct accgctgtgc tcagccggga gaccagtgcc aggttgctgg 600
ctggggcacc acggccgccc ggagagtgaa gtacaacaag ggcctgacct gctccagcat 660
cactatcctg agccctaaag agtgtgaggt cttctaccct ggcgtggtca ccaacaacat 720
gatatgtgct ggactggacc ggggccagga cccttgccag agtgactctg gaggcccccc 780
ggtctgtgac gagaccctcc aaggcatcct ctcgtggggt gtttaccccc gtggctctgc 840
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tga 1443

<210> 250
<211> 276
<212> PRT
<213> Homo sapiens

<400> 250
Met Arg Ala Pro His Leu His Leu Ser Ala Ala Ser Gly Ala Arg Ala
 1   5   10   15
Leu Ala Lys Leu Leu Pro Leu Leu Met Ala Gln Leu Trp Ala Ala Glu
            20   25   30
Ala Ala Leu Leu Pro Gln Asn Asp Thr Arg Leu Asp Pro Glu Ala Tyr
        35   40   45
Gly Ser Pro Cys Ala Arg Gly Ser Gln Pro Trp Gln Val Ser Leu Phe
    50   55   60
Asn Gly Leu Ser Phe His Cys Ala Gly Val Leu Val Asp Gln Ser Trp
65   70   75   80
Val Leu Thr Ala Ala His Cys Gly Asn Lys Pro Leu Trp Ala Arg Val
                85   90   95
Gly Asp Asp His Leu Leu Leu Leu Gln Gly Glu Gln Leu Arg Arg Thr
            100   105   110
Thr Arg Ser Val Val His Pro Lys Tyr His Gln Gly Ser Gly Pro Ile
        115   120   125
Leu Pro Arg Arg Thr Asp Glu His Asp Leu Met Leu Leu Lys Leu Ala
    130   135   140
Arg Pro Val Val Leu Gly Pro Arg Val Arg Ala Leu Gln Leu Pro Tyr
145   150   155   160
Arg Cys Ala Gln Pro Gly Asp Gln Cys Gln Val Ala Gly Trp Gly Thr
                165   170   175

```
Thr Ala Ala Arg Arg Val Lys Tyr Asn Lys Gly Leu Thr Cys Ser Ser
            180                 185                 190
Ile Thr Ile Leu Ser Pro Lys Glu Cys Glu Val Phe Tyr Pro Gly Val
        195                 200                 205
Val Thr Asn Asn Met Ile Cys Ala Gly Leu Asp Arg Gly Gln Asp Pro
    210                 215                 220
Cys Gln Ser Asp Ser Gly Gly Pro Leu Val Cys Asp Glu Thr Leu Gln
225                 230                 235                 240
Gly Ile Leu Ser Trp Gly Val Tyr Pro Cys Gly Ser Ala Gln His Pro
                245                 250                 255
Ala Val Tyr Thr Gln Ile Cys Lys Tyr Met Ser Trp Ile Asn Lys Val
            260                 265                 270
Ile Arg Ser Asn
        275
```

<210> 251
<211> 3226
<212> DNA
<213> Homo sapiens

<400> 251

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cgcgagctaa gcaggaggcg gaggcggagg cggagggcga ggggcgggga gcgccgcctg 60
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cagcaagatg gctttgaact cagggtcacc accagctatt ggaccttact atgaaaacca 180
tggataccaa ccggaaaacc cctatcccgc acagcccact gtggtcccca ctgtctacga 240
ggtgcatccg gctcagtact acccgtcccc cgtgccccag tacgccccga gggtcctgac 300
gcaggcttcc aaccccgtcg tctgcacgca gcccaaatcc ccatccggga cagtgtgcac 360
ctcaaagact aagaaagcac tgtgcatcac cttgaccctg gggaccttcc tcgtgggagc 420
tgcgctggcc gctggcctac tctggaagtt catgggcagc aagtgctcca actctgggat 480
agagtgcgac tcctcaggta cctgcatcaa cccctctaac tggtgtgatg gcgtgtcaca 540
ctgccccggc ggggaggacg agaatcggtg tgttcgcctc tacggaccaa acttcatcct 600
tcagatgtac tcatctcaga ggaagtcctg gcaccctgtg tgccaagacg actggaacga 660
gaactacggg cgggcggcct gcagggacat gggctataag aataattttt actctagcca 720
aggaatagtg gatgacagcg gatccaccag ctttatgaaa ctgaacacaa gtgccggcaa 780
tgtcgatatc tataaaaaac tgtaccacag tgatgcctgt tcttcaaaag cagtggtttc 840
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cggtgagagc gcgctcccgg gggcctggcc ctggcaggtc agcctgcacg tccagaacgt 960
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cgacctagtg aaaccagtgt gtctgcccaa cccaggcatg atgctgcagc cagaacagct 1260
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cctgatcaca ccagccatga tctgtgccgg cttcctgcag gggaacgtcg attcttgcca 1440
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ggtattcacg gactggattt atcgacaaat gagggcagac ggctaatcca catggtcttc 1620
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tagcagccct ggatggtggc cagaaataaa gggaccagcc cttcatgggt ggtgacgtgg 2160
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tagtcacttg taaggggaac agaaacattt ttgttcttat ggggtgagaa tatagacagt 2220
gcccttggtg cgagggaagc aattgaaaag gaacttgccc tgagcactcc tggtgcaggt 2280
ctccacctgc acattgggtg gggctcctgg gagggagact cagccttcct cctcatcctc 2340
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aagtctggca ccatgttggc ctcttcaggc ctgctagtca ctggaaattg aggtccatgg 2460
gggaaatcaa ggatgctcag tttaaggtac actgtttcca tgttatgttt ctacacattg 2520
ctacctcagt gctcctggaa acttagcttt tgatgtctcc aagtagtcca ccttcattta 2580
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acaaaatgac tggctcctga cttaacgttc tataaatgaa tgtgctgaag caaagtgccc 2700
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atgctgtggg tttccaacca ggggaagggt ccctttgca ttgccaagtg ccataaccat 2820
gagcactact ctaccatggt tctgcctcct ggccaagcag gctggtttgc aagaatgaaa 2880
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tggcactgta aggtgcttgc tccccaagac acatcctaaa aggtgttgta atggtgaaaa 3060
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<210> 252
<211> 492
<212> PRT
<213> Homo sapiens

<400> 252

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Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
 1               5                  10                  15
Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
            20                  25                  30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
        35                  40                  45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
    50                  55                  60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
65                  70                  75                  80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
                85                  90                  95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
            100                 105                 110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
        115                 120                 125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
    130                 135                 140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
145                 150                 155                 160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
                165                 170                 175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
            180                 185                 190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
        195                 200                 205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
    210                 215                 220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
225                 230                 235                 240
Cys Ile Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
                245                 250                 255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
```

```
            260                 265                 270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro
        275                 280                 285
Glu Trp Ile Val Thr Ala Ala His Cys Val Glu Lys Pro Leu Asn Asn
    290                 295                 300
Pro Trp His Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met
305                 310                 315                 320
Phe Tyr Gly Ala Gly Tyr Gln Val Glu Lys Val Ile Ser His Pro Asn
                325                 330                 335
Tyr Asp Ser Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln
            340                 345                 350
Lys Pro Leu Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn
        355                 360                 365
Pro Gly Met Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp
    370                 375                 380
Gly Ala Thr Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala
385                 390                 395                 400
Lys Val Leu Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr
                405                 410                 415
Asp Asn Leu Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly
            420                 425                 430
Asn Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser
        435                 440                 445
Lys Asn Asn Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly
    450                 455                 460
Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe
465                 470                 475                 480
Thr Asp Trp Ile Tyr Arg Gln Met Arg Ala Asp Gly
                485                 490
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<210> 253
<211> 1280
<212> DNA
<213> Homo sapiens

<400> 253

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tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 180
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300
ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420
tgccctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga 480
atgcctaccg tgctgcagtg cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag 540
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag 600
gactcctgca acggtgactc tgggggggcc ctgatctgca acgggtactt gcagggcctt 660
gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc 720
tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaactctg gggactggga 780
acccatgaaa ttgacccccа aatacatcct gcggaaggaa ttcaggaata tctgttccca 840
gcccctcctc cctcaggccc aggagtccag gcccccagcc cctcctccct caaaccaagg 900
gtacagatcc ccagcccctc ctccctcaga cccaggagtc cagacccccc agcccctcct 960
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tccaagcccc caacccctcc ttccccagac ccagaggtcc aggtcccagc ccctcctccc 1140
tcagacccag cggtccaatg ccacctagac tctccctgta cacagtgccc ccttgtggca 1200
cgttgaccca accttaccag ttggtttttc atttttgtc cctttcccct agatccagaa 1260
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ataaagtcta agagaagcgc 1280

<210> 254
<211> 254
<212> PRT
<213> Homo sapiens

<400> 254

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Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1               5                  10                  15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
            20                  25                  30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
        35                  40                  45
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
    50                  55                  60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
65                  70                  75                  80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                85                  90                  95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
            100                 105                 110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
        115                 120                 125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
    130                 135                 140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
145                 150                 155                 160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
                165                 170                 175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
            180                 185                 190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
        195                 200                 205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
    210                 215                 220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
225                 230                 235                 240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                245                 250
```

<210> 255
<211> 1391
<212> DNA
<213> Homo sapiens

<400> 255

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acctccctgc tgctgctggc gtcgacagcc atcctcaatg cggccaggat acctgttccc 180
ccagcctgtg ggaagcccca gcagctgaac cgggttgtgg gcggcgagga cagcactgac 240
agcgagtggc cctggatcgt gagcatccag aagaatggga cccaccactg cgcaggttct 300
ctgctcacca gccgctgggt gatcactgct gcccactgtt tcaaggacaa cctgaacaaa 360
ccatacctgt tctctgtgct gctgggggcc tggcagctgg ggaaccctgg ctctcggtcc 420
cagaaggtgg gtgttgcctg ggtggagccc caccctgtgt attcctggaa ggaaggtgcc 480
tgtgcagaca ttgccctggt gcgtctcgag cgctccatac agttctcaga gcgggtcctg 540
cccatctgcc tacctgatgc ctctatccac ctccctccaa acacccactg ctggatctca 600
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ggctggggga gcatccaaga tggagttccc ttgccccacc ctcagaccct gcagaagctg 660
aaggttccta tcatcgactc ggaagtctgc agccatctgt actggcgggg agcaggacag 720
ggacccatca ctgaggacat gctgtgtgcc ggctacttgg agggggagcg ggatgcttgt 780
ctgggcgact ccgggggccc cctcatgtgc caggtggacg gcgcctggct gctggccggc 840
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ccagtgaaaa a 1391

<210> 256
<211> 317
<212> PRT
<213> Homo sapiens

<400> 256
Met Val Val Ser Gly Ala Pro Pro Ala Leu Gly Gly Gly Cys Leu Gly
 1   5   10   15
Thr Phe Thr Ser Leu Leu Leu Leu Ala Ser Thr Ala Ile Leu Asn Ala
            20   25   30
Ala Arg Ile Pro Val Pro Pro Ala Cys Gly Lys Pro Gln Gln Leu Asn
        35   40   45
Arg Val Val Gly Gly Glu Asp Ser Thr Asp Ser Glu Trp Pro Trp Ile
    50   55   60
Val Ser Ile Gln Lys Asn Gly Thr His His Cys Ala Gly Ser Leu Leu
65   70   75   80
Thr Ser Arg Trp Val Ile Thr Ala Ala His Cys Phe Lys Asp Asn Leu
                85   90   95
Asn Lys Pro Tyr Leu Phe Ser Val Leu Leu Gly Ala Trp Gln Leu Gly
            100   105   110
Asn Pro Gly Ser Arg Ser Gln Lys Val Gly Val Ala Trp Val Glu Pro
        115   120   125
His Pro Val Tyr Ser Trp Lys Glu Gly Ala Cys Ala Asp Ile Ala Leu
    130   135   140
Val Arg Leu Glu Arg Ser Ile Gln Phe Ser Glu Arg Val Leu Pro Ile
145   150   155   160
Cys Leu Pro Asp Ala Ser Ile His Leu Pro Pro Asn Thr His Cys Trp
                165   170   175
Ile Ser Gly Trp Gly Ser Ile Gln Asp Gly Val Pro Leu Pro His Pro
            180   185   190
Gln Thr Leu Gln Lys Leu Lys Val Pro Ile Ile Asp Ser Glu Val Cys
        195   200   205
Ser His Leu Tyr Trp Arg Gly Ala Gly Gln Gly Pro Ile Thr Glu Asp
    210   215   220
Met Leu Cys Ala Gly Tyr Leu Glu Gly Glu Arg Asp Ala Cys Leu Gly
225   230   235   240
Asp Ser Gly Gly Pro Leu Met Cys Gln Val Asp Gly Ala Trp Leu Leu
                245   250   255
Ala Gly Ile Ile Ser Trp Gly Glu Gly Cys Ala Glu Arg Asn Arg Pro
            260   265   270
Gly Val Tyr Ile Ser Leu Ser Ala His Arg Ser Trp Val Glu Lys Ile
        275   280   285
Val Gln Gly Val Gln Leu Arg Gly Arg Ala Gln Gly Gly Gly Ala Leu

```
    290                 295                 300
Arg Ala Pro Ser Gln Gly Ser Gly Ala Ala Arg Ser
305                 310                 315
```

<210> 257
<211> 1184
<212> DNA
<213> Homo sapiens

<400> 257
atctgccacg atgttgctgc tcagcctgac cctaagcctg gttctcctcg gctcctcctg 60
gggctgcggc attcctgcca tcaaaccggc actgagcttc agccagagga ttgtcaacgg 120
ggagaatgca gtgttgggct cctggccctg gcaggtgtcc ctgcaggaca gcagcggctt 180
ccacttctgc ggtggttctc tcatcagcca gtcctgggtg gtcactgctg cccactgcaa 240
tgtcagccct ggccgccatt ttgttgtcct gggcgagtat gaccgatcat caaacgcaga 300
gcccttgcag gttctgtccg tctctcgggc cattacacac cctagctgga actctaccac 360
catgaacaat gacgtgacgc tgctgaagct cgcctcgcca gcccagtaca caacacgcat 420
ctcgccagtt tgcctggcat cctcaaacga ggctctgact gaaggcctca cgtgtgtcac 480
caccggctgg ggtcgcctca gtggcgtggg caatgtgaca ccagcacatc tgcagcaggt 540
ggctttgccc ctggtcactg tgaatcagtg ccggcagtac tggggctcaa gtatcactga 600
ctccatgatc tgtgcaggtg gcgcaggtgc ctcctcgtgc cagggtgact ccggaggccc 660
tcttgtctgc cagaagggaa acacatgggt gcttattggt attgtctcct ggggcaccaa 720
aaactgcaat gtgcgcgcac ctgctgtgta tactcgagtt agcaagttca gcacctggat 780
caaccaggtc atagcctaca actgagctca ccacaggccc tccccagctc aacccattaa 840
agacccaggc cctgtcccat catgcattca tgtctgtctt cctggctcag gagaaagaag 900
aggctgttga gggtccgact ccctacttgg acttctggca cagaaggggc tgagtgactc 960
cttgagtagc agtggctctt cctagagtag ccatgccgag gccggggccc ccacccctcc 1020
tccagggcaa ccccttggtc ctacagcaag aagccagaac tgttggaatg aatggcagcc 1080
ctccctggag aggcagcctg tttactgaat acagaggata cgtttacaaa ctgaatacgc 1140
ataataaata actgcacatt ctccatccaa aaaaaaaaaa aaaa 1184

<210> 258
<211> 264
<212> PRT
<213> Homo sapiens

<400> 258
```
Met Leu Leu Leu Ser Leu Thr Leu Ser Leu Val Leu Leu Gly Ser Ser
 1               5                  10                  15
Trp Gly Cys Gly Ile Pro Ala Ile Lys Pro Ala Leu Ser Phe Ser Gln
            20                  25                  30
Arg Ile Val Asn Gly Glu Asn Ala Val Leu Gly Ser Trp Pro Trp Gln
        35                  40                  45
Val Ser Leu Gln Asp Ser Ser Gly Phe His Phe Cys Gly Gly Ser Leu
    50                  55                  60
Ile Ser Gln Ser Trp Val Val Thr Ala Ala His Cys Asn Val Ser Pro
65                  70                  75                  80
Gly Arg His Phe Val Val Leu Gly Glu Tyr Asp Arg Ser Ser Asn Ala
                85                  90                  95
Glu Pro Leu Gln Val Leu Ser Val Ser Arg Ala Ile Thr His Pro Ser
            100                 105                 110
Trp Asn Ser Thr Thr Met Asn Asn Asp Val Thr Leu Leu Lys Leu Ala
        115                 120                 125
Ser Pro Ala Gln Tyr Thr Thr Arg Ile Ser Pro Val Cys Leu Ala Ser
    130                 135                 140
Ser Asn Glu Ala Leu Thr Glu Gly Leu Thr Cys Val Thr Thr Gly Trp
145                 150                 155                 160
```

```
Gly Arg Leu Ser Gly Val Gly Asn Val Thr Pro Ala His Leu Gln Gln
                165                 170                 175
Val Ala Leu Pro Leu Val Thr Val Asn Gln Cys Arg Gln Tyr Trp Gly
            180                 185                 190
Ser Ser Ile Thr Asp Ser Met Ile Cys Ala Gly Gly Ala Gly Ala Ser
        195                 200                 205
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Gly Asn
    210                 215                 220
Thr Trp Val Leu Ile Gly Ile Val Ser Trp Gly Thr Lys Asn Cys Asn
225                 230                 235                 240
Val Arg Ala Pro Ala Val Tyr Thr Arg Val Ser Lys Phe Ser Thr Trp
                245                 250                 255
Ile Asn Gln Val Ile Ala Tyr Asn
            260
```

<210> 259
<211> 1207
<212> DNA
<213> Homo sapiens

<400> 259
ggagtgcagg cttggaaagc aggagagctc agcctacgtc tttaatcctc ctgcccaccc 60
cttggattct gtctccactg ggactcaaga gaggaacctg gggcccgctc ctccccccctc 120
caggccatga ggattctgca gttaatcctg cttgctctgg caacagggct tgtaggggga 180
gagaccagga tcatcaaggg gttcgagtgc aagcctcact cccagccctg gcaggcagcc 240
ctgttcgaga agacgcggct actctgtggg gcgacgctca tcgcccccag atggctcctg 300
acagcagccc actgcctcaa gccccgctac atagttcacc tggggcagca caacctccag 360
aaggaggagg gctgtgagca gacccggaca gccactgagt ccttccccca ccccggcttc 420
aacaacagcc tccccaacaa agaccaccgc aatgacatca tgctggtgaa gatggcatcg 480
ccagtctcca tcacctgggc tgtgcgaccc ctcaccctct cctcacgctg tgtcactgct 540
ggcaccagct gcctcatttc cggctggggc agcacgtcca gccccagtt acgcctgcct 600
cacaccttgc gatgcgccaa catcaccatc attgagcacc agaagtgtga gaacgcctac 660
cccggcaaca tcacagacac catggtgtgt gccagcgtgc aggaaggggg caaggactcc 720
tgccagggtg actccggggg ccctctggtc tgtaaccagt ctcttcaagg cattatctcc 780
tggggccagg atccgtgtgc gatcacccga aagcctggtg tctacacgaa agtctgcaaa 840
tatgtggact ggatccagga gacgatgaag aacaattaga ctggacccac ccaccacagc 900
ccatcaccct ccatttccac ttggtgtttg gttcctgttc actctgttaa taagaaaccc 960
taagccaaga ccctctacga acattctttg ggcctcctgg actacaggag atgctgtcac 1020
ttaataatca acctggggtt cgaaatcagt gagacctgga ttcaaattct gccttgaaat 1080
attgtgactc tgggaatgac aacacctggt ttgttctctg ttgtatcccc agccccaaag 1140
acagctcctg gccatatatc aaggtttcaa taaatatttg ctaaatgagt gaaaaaaaaa 1200
aaaaaaa   1207

<210> 260
<211> 250
<212> PRT
<213> Homo sapiens

<400> 260
```
Met Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val
 1               5                  10                  15
Gly Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser
            20                  25                  30
Gln Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly
        35                  40                  45
Ala Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu
    50                  55                  60
```

```
Lys Pro Arg Tyr Ile Val His Leu Gly Gln His Asn Leu Gln Lys Glu
65                  70                  75                  80
Glu Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro
                85                  90                  95
Gly Phe Asn Asn Ser Leu Pro Asn Lys Asp His Arg Asn Asp Ile Met
            100                 105                 110
Leu Val Lys Met Ala Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro
        115                 120                 125
Leu Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile
    130                 135                 140
Ser Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr
145                 150                 155                 160
Leu Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn
                165                 170                 175
Ala Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln
            180                 185                 190
Glu Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
        195                 200                 205
Cys Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys
    210                 215                 220
Ala Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val
225                 230                 235                 240
Asp Trp Ile Gln Glu Thr Met Lys Asn Asn
                245                 250
```

<210> 261
<211> 1289
<212> DNA
<213> Homo sapiens

<400> 261

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ctgccttgct ccacacctgg tcaggggaga gaggggagga aagccaaggg aagggaccta 60
actgaaaaca aacaagctgg gagaagcagg aatctgcgct cgggttccgc agatgcagag 120
gttgaggtgg ctgcgggact ggaagtcatc gggcagaggt ctcacagcag ccaaggaacc 180
tggggcccgc tcctcccccc tccaggccat gaggattctg cagttaatcc tgcttgctct 240
ggcaacaggg cttgtagggg gagagaccag gatcatcaag gggttcgagt gcaagcctca 300
ctcccagccc tggcaggcag ccctgttcga gaagacgcgg ctactctgtg gggcgacgct 360
catcgccccc agatggctcc tgacagcagc ccactgcctc aagccccgct acatagttca 420
cctggggcag cacaacctcc agaaggagga gggctgtgag cagacccgga cagccactga 480
gtccttcccc caccccggct tcaacaacag cctccccaac aaagaccacc gcaatgacat 540
catgctggtg aagatggcat cgccagtctc catcacctgg gctgtgcgac ccctcaccct 600
ctcctcacgc tgtgtcactg ctggcaccag ctgcctcatt tccggctggg gcagcacgtc 660
cagcccccag ttacgcctgc ctcacacctt gcgatgcgcc aacatcacca tcattgagca 720
ccagaagtgt gagaacgcct accccggcaa catcacagac accatggtgt gtgccagcgt 780
gcaggaaggg ggcaaggact cctgccaggg tgactccggg ggccctctgg tctgtaacca 840
gtctcttcaa ggcattatct cctggggcca ggatccgtgt gcgatcaccc gaaagcctgg 900
tgtctacacg aaagtctgca aatatgtgga ctggatccag gagacgatga agaacaatta 960
gactggaccc acccaccaca gcccatcacc ctccatttcc acttggtgtt tggttcctgt 1020
tcactctgtt aataagaaac cctaagccaa gaccctctac gaacattctt tgggcctcct 1080
ggactacagg agatgctgtc acttaataat caacctgggg ttcgaaatca gtgagacctg 1140
gattcaaatt ctgccttgaa atattgtgac tctgggaatg acaacacctg gtttgttctc 1200
tgttgtatcc ccagccccaa agacagctcc tggccatata tcaaggtttc aataaatatt 1260
tgctaaatga gtgaaaaaaa aaaaaaaaa                                    1289
```

<210> 262
<211> 282
<212> PRT

<213> Homo sapiens

<400> 262

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Met Gln Arg Leu Arg Trp Leu Arg Asp Trp Lys Ser Ser Gly Arg Gly
 1               5                  10                  15
Leu Thr Ala Ala Lys Glu Pro Gly Ala Arg Ser Ser Pro Leu Gln Ala
            20                  25                  30
Met Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val
        35                  40                  45
Gly Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser
    50                  55                  60
Gln Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly
65                  70                  75                  80
Ala Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu
                85                  90                  95
Lys Pro Arg Tyr Ile Val His Leu Gly Gln His Asn Leu Gln Lys Glu
            100                 105                 110
Glu Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro
        115                 120                 125
Gly Phe Asn Asn Ser Leu Pro Asn Lys Asp His Arg Asn Asp Ile Met
    130                 135                 140
Leu Val Lys Met Ala Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro
145                 150                 155                 160
Leu Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile
                165                 170                 175
Ser Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr
            180                 185                 190
Leu Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn
        195                 200                 205
Ala Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln
    210                 215                 220
Glu Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
225                 230                 235                 240
Cys Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys
                245                 250                 255
Ala Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val
            260                 265                 270
Asp Trp Ile Gln Glu Thr Met Lys Asn Asn
        275                 280
```

<210> 263
<211> 802
<212> DNA
<213> Homo sapiens

<400> 263

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accaccatga atctacttct gatccttacc tttgttgcag ctgctgttgc tgcccccttt 60
gatgatgatg acaagatcgt tgggggctac atctgtgagg agaattctgt cccctaccag 120
gtgtccttga attctggcta ccacttctgc ggtggctccc tcatcagcga acagtgggtg 180
gtgtcagcag gtcactgcta caagtcccgc atccaggtga gactgggaga gcacaacatc 240
gaagtcctgg aggggaatga acagttcatc aatgcagcca agatcatccg ccaccccaaa 300
tacaacagcc ggactctgga caatgacatc ctgctgatca agctctcctc acctgccgtc 360
atcaattccc gcgtgtccgc catctctctg cccactgccc ctccagctgc tggcaccgag 420
tccctcatct ccggctgggg caacactctg agttctggtg ccgactaccc agacgagctg 480
cagtgcctgg atgctcctgt gctgagccag gctgagtgtg aagcctccta ccctggaaag 540
attaccaaca acatgttctg tgtgggcttc ctcgagggag gcaaggattc ctgccagggt 600
gattctggtg gccctgtggt ctccaatgga gagctccaag gaattgtctc ctggggctat 660
```

ggctgtgccc agaagaacag gcctggagtc tacaccaagg tctacaacta tgtggactgg 720
attaaggaca ccatagctgc caacagctaa agcccctggt ccctctgcag tctctatacc 780
aataaagtga ccctgctctc ac 802

<210> 264
<211> 247
<212> PRT
<213> Homo sapiens

<400> 264

Met	Asn	Leu	Leu	Leu	Ile	Leu	Thr	Phe	Val	Ala	Ala	Ala	Val	Ala	Ala
1				5				10					15		
Pro	Phe	Asp	Asp	Asp	Asp	Lys	Ile	Val	Gly	Gly	Tyr	Ile	Cys	Glu	Glu
			20					25					30		
Asn	Ser	Val	Pro	Tyr	Gln	Val	Ser	Leu	Asn	Ser	Gly	Tyr	His	Phe	Cys
		35					40					45			
Gly	Gly	Ser	Leu	Ile	Ser	Glu	Gln	Trp	Val	Val	Ser	Ala	Gly	His	Cys
	50					55					60				
Tyr	Lys	Ser	Arg	Ile	Gln	Val	Arg	Leu	Gly	Glu	His	Asn	Ile	Glu	Val
65					70					75					80
Leu	Glu	Gly	Asn	Glu	Gln	Phe	Ile	Asn	Ala	Ala	Lys	Ile	Ile	Arg	His
				85					90					95	
Pro	Lys	Tyr	Asn	Ser	Arg	Thr	Leu	Asp	Asn	Asp	Ile	Leu	Leu	Ile	Lys
			100					105					110		
Leu	Ser	Ser	Pro	Ala	Val	Ile	Asn	Ser	Arg	Val	Ser	Ala	Ile	Ser	Leu
		115					120					125			
Pro	Thr	Ala	Pro	Pro	Ala	Ala	Gly	Thr	Glu	Ser	Leu	Ile	Ser	Gly	Trp
	130					135					140				
Gly	Asn	Thr	Leu	Ser	Ser	Gly	Ala	Asp	Tyr	Pro	Asp	Glu	Leu	Gln	Cys
145					150					155					160
Leu	Asp	Ala	Pro	Val	Leu	Ser	Gln	Ala	Glu	Cys	Glu	Ala	Ser	Tyr	Pro
				165					170					175	
Gly	Lys	Ile	Thr	Asn	Asn	Met	Phe	Cys	Val	Gly	Phe	Leu	Glu	Gly	Gly
			180					185					190		
Lys	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Val	Val	Ser	Asn	Gly
		195					200					205			
Glu	Leu	Gln	Gly	Ile	Val	Ser	Trp	Gly	Tyr	Gly	Cys	Ala	Gln	Lys	Asn
	210					215					220				
Arg	Pro	Gly	Val	Tyr	Thr	Lys	Val	Tyr	Asn	Tyr	Val	Asp	Trp	Ile	Lys
225					230					235					240
Asp	Thr	Ile	Ala	Ala	Asn	Ser									
				245											

<210> 265
<211> 1475
<212> DNA
<213> Homo sapiens

<400> 265
acctgccgcc atcttgctca ccagcctcca aaatgcggct ggggctcctg agcgtggcgc 60
tgttgtttgt ggggagctct cacttatact cagaccacta ctcgccctct ggaaggcaca 120
ggctcggccc ctcgccggaa ccggcggcta gttcccagca ggctgaggcc gtccgcaaga 180
ggctccggcg gcggagggag ggaggggcgc atgcaaagga ttgtggaaca gcaccgctta 240
aggatgtgtt gcaagggtct cggattatag ggggcaccga agcacaagct ggcgcatggc 300
cgtgggtggt gagcctgcag attaaatatg gccgtgttct tgttcatgta tgtgggggaa 360
ccctagtgag agagaggtgg gtcctcacag ctgcccactg cactaaagac gctagcgatc 420
ctttaatgtg gacagctgtg attggaacta ataatataca tggacgctat cctcatacca 480

agaagataaa aattaaagca atcattattc atccaaactt cattttggaa tcttatgtaa 540
atgatattgc acttttttcac ttaaaaaaag cagtgaggta taatgactat attcagccta 600
tttgcctacc ttttgatgtt ttccaaatcc tggacggaaa cacaaagtgt tttataagtg 660
gctggggaag aacaaaagaa gaaggtaacg ctacaaatat tttacaagat gcagaagtgc 720
attatatttc tcgagagatg tgtaattctg agaggagtta tgggggaata attcctaaca 780
cttcattttg tgcaggtgat gaagatggag cttttgatac ttgcaggggt gacagtgggg 840
gaccattaat gtgctactta ccagaatata aaagattttt tgtaatggga attaccagtt 900
acggacatgg ctgtggtcga agaggttttc ctggtgtcta tattgggcca tccttctacc 960
aaaagtggct gacagagcat ttcttccatg caagcactca aggcatactt actataaata 1020
ttttacgtgg ccagatcctc atagctttat gttttgtcat cttactagca acaacataaa 1080
gaaattctga aggctttcat atctttattt tgcattgtgt ccctttctat gttctatata 1140
atgaacatca tttattcttc tagcaattaa ttgcctacat tagagatttc atgtgaacat 1200
tttatgggct ataagtattg tgacagatat acaattgtaa ttttggcact gaatcacatg 1260
tctccttgaa atatcttgat tattttataa tcataattct gtatctggaa tactcataga 1320
gtttgtacaa aatattcagt taaacatata tgtgtataaa tgccaaataa tagtttataa 1380
ttaaaatgaa agctgtcatt tggttaaatt aataaaaatt ctttcttaga ttttattcta 1440
aaaaaaaaaa aaaaaaaaga aaaaaaaaaa aaaaa 1475

<210> 266
<211> 348
<212> PRT
<213> Homo sapiens

<400> 266

Met	Arg	Leu	Gly	Leu	Leu	Ser	Val	Ala	Leu	Leu	Phe	Val	Gly	Ser	Ser
1				5				10						15	
His	Leu	Tyr	Ser	Asp	His	Tyr	Ser	Pro	Ser	Gly	Arg	His	Arg	Leu	Gly
			20					25					30		
Pro	Ser	Pro	Glu	Pro	Ala	Ala	Ser	Ser	Gln	Gln	Ala	Glu	Ala	Val	Arg
		35					40					45			
Lys	Arg	Leu	Arg	Arg	Arg	Arg	Glu	Gly	Gly	Ala	His	Ala	Lys	Asp	Cys
	50					55					60				
Gly	Thr	Ala	Pro	Leu	Lys	Asp	Val	Leu	Gln	Gly	Ser	Arg	Ile	Ile	Gly
65					70					75					80
Gly	Thr	Glu	Ala	Gln	Ala	Gly	Ala	Trp	Pro	Trp	Val	Val	Ser	Leu	Gln
				85					90					95	
Ile	Lys	Tyr	Gly	Arg	Val	Leu	Val	His	Val	Cys	Gly	Gly	Thr	Leu	Val
			100					105					110		
Arg	Glu	Arg	Trp	Val	Leu	Thr	Ala	Ala	His	Cys	Thr	Lys	Asp	Ala	Ser
		115					120					125			
Asp	Pro	Leu	Met	Trp	Thr	Ala	Val	Ile	Gly	Thr	Asn	Asn	Ile	His	Gly
	130					135					140				
Arg	Tyr	Pro	His	Thr	Lys	Lys	Ile	Lys	Ile	Lys	Ala	Ile	Ile	Ile	His
145					150					155					160
Pro	Asn	Phe	Ile	Leu	Glu	Ser	Tyr	Val	Asn	Asp	Ile	Ala	Leu	Phe	His
				165					170					175	
Leu	Lys	Lys	Ala	Val	Arg	Tyr	Asn	Asp	Tyr	Ile	Gln	Pro	Ile	Cys	Leu
			180					185					190		
Pro	Phe	Asp	Val	Phe	Gln	Ile	Leu	Asp	Gly	Asn	Thr	Lys	Cys	Phe	Ile
		195					200					205			
Ser	Gly	Trp	Gly	Arg	Thr	Lys	Glu	Glu	Gly	Asn	Ala	Thr	Asn	Ile	Leu
	210					215					220				
Gln	Asp	Ala	Glu	Val	His	Tyr	Ile	Ser	Arg	Glu	Met	Cys	Asn	Ser	Glu
225					230					235					240
Arg	Ser	Tyr	Gly	Gly	Ile	Ile	Pro	Asn	Thr	Ser	Phe	Cys	Ala	Gly	Asp
				245					250					255	
Glu	Asp	Gly	Ala	Phe	Asp	Thr	Cys	Arg	Gly	Asp	Ser	Gly	Gly	Pro	Leu
			260					265					270		

```
Met Cys Tyr Leu Pro Glu Tyr Lys Arg Phe Phe Val Met Gly Ile Thr
        275                 280                 285
Ser Tyr Gly His Gly Cys Gly Arg Arg Gly Phe Pro Gly Val Tyr Ile
    290                 295                 300
Gly Pro Ser Phe Tyr Gln Lys Trp Leu Thr Glu His Phe Phe His Ala
305                 310                 315                 320
Ser Thr Gln Gly Ile Leu Thr Ile Asn Ile Leu Arg Gly Gln Ile Leu
                325                 330                 335
Ile Ala Leu Cys Phe Val Ile Leu Leu Ala Thr Thr
            340                 345
```

<210> 267
<211> 1164
<212> DNA
<213> Homo sapiens

<400> 267
atgattgccg ttctcattgt gttgtccctg acagtggtgg cagtgaccat aggtctcctg 60
gttcacttcc tagtatttga ccaaaaaaag gagtactatc atggctcctt taaaatttta 120
gatccacaaa tcaataacaa tttcggacaa agcaacacat atcaacttaa ggacttacga 180
gagacgaccg aaaatttggt ggatgagata tttatagatt cagcctggaa gaaaaattat 240
atcaagaacc aagtagtcag actgactcca gaggaagatg gtgtgaaagt agatgtcatt 300
atggtgttcc agttcccctc tactgaacaa agggcagtaa gagagaagaa aatccaaagc 360
atcttaaatc agaagataag gaatttaaga gccttgccaa taaatgcctc atcagttcaa 420
gttaatggtt gtggtaaacg agttgttcca ttaaacgtca acagaatagc atctggagtc 480
attgcaccca aggcggcctg gccttggcaa gcttcccttc agtatgataa catccatcag 540
tgtggggcca ccttgattag taacacatgg cttgtcactg cagcacactg cttccagaag 600
tataaaaatc cacatcaatg gactgttagt tttggaacaa aaatcaaccc tcccttaatg 660
aaaagaaatg tcagaagatt tattatccat gagaagtacc gctctgcagc aagagagtac 720
gacattgctg ttgtgcaggt ctcttccaga gtcacctttt cggatgacat acgccagatt 780
tgtttgccag aagcctctgc atccttccaa ccaaatttga ctgtccacat cacaggattt 840
ggagcacttt actatggtgg ggaatcccaa aatgatctcc gagaagccag agtgaaaatc 900
ataagtgatg atgtctgcaa gcaaccacag gtgtatggca atgatataaa acctggaatg 960
ttctgtgccg gatatatgga aggaatttat gatgcctgca ggggtgattc tgggggacct 1020
ttagtcacaa gggatctgaa agatacgtgg tatctcattg gaattgtaag ctggggagat 1080
aactgtggtc aaaaggacaa gcctggagtc tacacacaag tgacttatta ccgaaactgg 1140
attgcttcaa aaacaggcat ctaa   1164

<210> 268
<211> 387
<212> PRT
<213> Homo sapiens

<400> 268
```
Met Ile Ala Val Leu Ile Val Leu Ser Leu Thr Val Val Ala Val Thr
 1               5                  10                  15
Ile Gly Leu Leu Val His Phe Leu Val Phe Asp Gln Lys Lys Glu Tyr
            20                  25                  30
Tyr His Gly Ser Phe Lys Ile Leu Asp Pro Gln Ile Asn Asn Asn Phe
        35                  40                  45
Gly Gln Ser Asn Thr Tyr Gln Leu Lys Asp Leu Arg Glu Thr Thr Glu
    50                  55                  60
Asn Leu Val Asp Glu Ile Phe Ile Asp Ser Ala Trp Lys Lys Asn Tyr
65                  70                  75                  80
Ile Lys Asn Gln Val Val Arg Leu Thr Pro Glu Glu Asp Gly Val Lys
                85                  90                  95
Val Asp Val Ile Met Val Phe Gln Phe Pro Ser Thr Glu Gln Arg Ala
```

```
                100                 105                 110
Val Arg Glu Lys Lys Ile Gln Ser Ile Leu Asn Gln Lys Ile Arg Asn
            115                 120                 125
Leu Arg Ala Leu Pro Ile Asn Ala Ser Ser Val Gln Val Asn Gly Cys
        130                 135                 140
Gly Lys Arg Val Val Pro Leu Asn Val Asn Arg Ile Ala Ser Gly Val
145                 150                 155                 160
Ile Ala Pro Lys Ala Ala Trp Pro Trp Gln Ala Ser Leu Gln Tyr Asp
                165                 170                 175
Asn Ile His Gln Cys Gly Ala Thr Leu Ile Ser Asn Thr Trp Leu Val
            180                 185                 190
Thr Ala Ala His Cys Phe Gln Lys Tyr Lys Asn Pro His Gln Trp Thr
        195                 200                 205
Val Ser Phe Gly Thr Lys Ile Asn Pro Pro Leu Met Lys Arg Asn Val
    210                 215                 220
Arg Arg Phe Ile Ile His Glu Lys Tyr Arg Ser Ala Ala Arg Glu Tyr
225                 230                 235                 240
Asp Ile Ala Val Val Gln Val Ser Ser Arg Val Thr Phe Ser Asp Asp
                245                 250                 255
Ile Arg Gln Ile Cys Leu Pro Glu Ala Ser Ala Ser Phe Gln Pro Asn
            260                 265                 270
Leu Thr Val His Ile Thr Gly Phe Gly Ala Leu Tyr Tyr Gly Gly Glu
        275                 280                 285
Ser Gln Asn Asp Leu Arg Glu Ala Arg Val Lys Ile Ile Ser Asp Asp
    290                 295                 300
Val Cys Lys Gln Pro Gln Val Tyr Gly Asn Asp Ile Lys Pro Gly Met
305                 310                 315                 320
Phe Cys Ala Gly Tyr Met Glu Gly Ile Tyr Asp Ala Cys Arg Gly Asp
                325                 330                 335
Ser Gly Gly Pro Leu Val Thr Arg Asp Leu Lys Asp Thr Trp Tyr Leu
            340                 345                 350
Ile Gly Ile Val Ser Trp Gly Asp Asn Cys Gly Gln Lys Asp Lys Pro
        355                 360                 365
Gly Val Tyr Thr Gln Val Thr Tyr Tyr Arg Asn Trp Ile Ala Ser Lys
    370                 375                 380
Thr Gly Ile
385
```

<210> 269
<211> 431
<212> PRT
<213> Rattus norvegicus

<400> 269

```
Met Ala Arg Gly Gln Pro Arg Arg Ser Glu Glu Pro Trp Thr Ala Leu
 1               5                  10                  15
Arg Asn Arg Thr Glu Cys Lys Thr Lys Ile Lys Leu Thr Lys Cys Gly
            20                  25                  30
Lys Ile Thr Leu Gly Ile Leu Thr Ala Val Ile Ala Ala Val Val Ile
        35                  40                  45
Gly Leu Ile Ala Tyr Phe Ala Ala Cys Gly Lys Thr Pro Phe Tyr Tyr
    50                  55                  60
His Val Ser Phe Lys Val Asn Asn Ile Asp Tyr Asp Ser Lys Phe Ala
65                  70                  75                  80
Lys Pro Tyr Ser Gln Glu Tyr Met Asp Leu Asn Lys Arg Ile Val Ser
                85                  90                  95
Leu Met Asn Glu Thr Phe His Glu Ser Lys Leu Arg Lys Gln Tyr Val
```

```
            100                 105                 110
Lys Ala His Thr Val Gln Val Ser Lys Ala Lys Gly Lys Val Val Ile
        115                 120                 125
His Gly Val Leu Lys Phe Lys Ser Cys Tyr Lys Asn Asn Val Glu Lys
    130                 135                 140
Phe Trp Asp Ser Val Glu Thr Ile Leu Tyr Gln Lys Leu Lys Ser Gln
145                 150                 155                 160
Thr Arg Leu Leu Ile Asp Ser Ser Ser Phe Lys Phe Ser Asp Ile Ala
                165                 170                 175
Met Pro Ile Ala Glu Asp Leu Leu Asn Thr Cys Cys Gly Arg Arg Thr
            180                 185                 190
Ile Thr Pro Gly Gly His Lys Val Ala Gly Gly Gln Asp Ala Glu Glu
        195                 200                 205
Gly Glu Trp Pro Trp Gln Ala Ser Leu Gln Gln Asn Asn Val His Arg
    210                 215                 220
Cys Gly Ala Thr Leu Ile Ser Asn Ser Trp Leu Ile Thr Ala Ala His
225                 230                 235                 240
Cys Phe Val Arg Ser Ala Asn Pro Lys Asp Trp Lys Val Ser Phe Gly
                245                 250                 255
Phe Leu Leu Ser Lys Pro Gln Ala Gln Arg Ala Val Lys Ser Ile Val
            260                 265                 270
Ile His Glu Asn Tyr Ser Tyr Pro Ala His Asn Asn Asp Ile Ala Val
        275                 280                 285
Val Arg Leu Ser Ser Pro Val Leu Tyr Glu Asn Asn Ile Arg Arg Ala
    290                 295                 300
Cys Leu Pro Glu Ala Thr Gln Lys Phe Pro Pro Asn Ser Asp Val Val
305                 310                 315                 320
Val Thr Gly Trp Gly Thr Leu Lys Ser Asp Gly Asp Ser Pro Asn Ile
                325                 330                 335
Leu Gln Lys Gly Arg Val Lys Ile Ile Asp Asn Lys Thr Cys Asn Ser
            340                 345                 350
Gly Lys Ala Tyr Gly Gly Val Ile Thr Pro Gly Met Leu Cys Ala Gly
        355                 360                 365
Phe Leu Glu Gly Arg Val Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro
    370                 375                 380
Leu Val Ser Glu Asp Ser Lys Gly Ile Trp Phe Leu Ala Gly Ile Val
385                 390                 395                 400
Ser Trp Gly Asp Glu Cys Ala Leu Pro Asn Lys Pro Gly Val Tyr Thr
                405                 410                 415
Arg Val Thr His Tyr Arg Asp Trp Ile Ser Ser Lys Thr Gly Leu
            420                 425                 430
```

<210> 270
<211> 247
<212> PRT
<213> Homo sapiens

<400> 270

```
Met Asn Pro Leu Leu Ile Leu Ala Phe Val Gly Ala Ala Val Ala Val
 1               5                  10                  15
Pro Phe Asp Asp Asp Asp Lys Ile Val Gly Gly Tyr Thr Cys Glu Glu
            20                  25                  30
Asn Ser Val Pro Tyr Gln Val Ser Leu Asn Ser Gly Ser His Phe Cys
        35                  40                  45
Gly Gly Ser Leu Ile Ser Glu Gln Trp Val Val Ser Ala Gly His Cys
    50                  55                  60
Tyr Lys Pro His Ile Gln Val Arg Leu Gly Glu His Asn Ile Glu Val
```

```
65                  70                  75                  80
Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile Ile Arg His
                85                  90                  95
Pro Lys Tyr Asn Arg Ile Thr Leu Asn Asn Asp Ile Met Leu Ile Lys
            100                 105                 110
Leu Ser Thr Pro Ala Val Ile Asn Ala His Val Ser Thr Ile Ser Leu
        115                 120                 125
Pro Thr Ala Pro Pro Ala Ala Gly Thr Glu Cys Leu Ile Ser Gly Trp
    130                 135                 140
Gly Asn Thr Leu Ser Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys
145                 150                 155                 160
Leu Asp Ala Pro Val Leu Thr Gln Ala Lys Cys Lys Ala Ser Tyr Pro
                165                 170                 175
Leu Lys Ile Thr Ser Lys Met Phe Cys Val Gly Phe Leu Glu Gly Gly
            180                 185                 190
Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Val Val Cys Asn Gly
        195                 200                 205
Gln Leu Gln Gly Ile Val Ser Trp Gly Tyr Gly Cys Ala Gln Lys Arg
    210                 215                 220
Arg Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Asp Trp Ile Lys
225                 230                 235                 240
Asp Thr Ile Ala Ala Asn Ser
                245
```

<210> 271
<211> 1099
<212> DNA
<213> Homo sapiens

<400> 271

```
gcacagccca gggccatgct cctgttctca gtgttgctgc tcctgtccct ggtcacggga 60
actcagctcg gtccacggac tcctctccca gaggctggag tggctatcct aggcagggct 120
aggggagccc accgccctca gccccgtcat ccccccagcc cagtcagtga atgtggtgac 180
agatctattt tcgagggaag aactcggtat tccagaatca caggggggat ggaggcggag 240
gtgggtgagt ttccgtggca ggtgagtatt caggcaagaa gtgaaccttt ctgtggcggc 300
tccatcctca acaagtggtg gattctcact gcggctcact gcttatattc cgaggagctg 360
tttccagaag aactgagtgt cgtgctgggg accaacgact taactagccc atccatggaa 420
ataaaggagg tcgccagcat cattcttcac aaagacttta agagagccaa catggacaat 480
gacattgcct tgctgctgct ggcttcgccc atcaagctcg atgacctgaa ggtgcccatc 540
tgcctccccа cgcagccccgg ccctgccaca tggcgcgaat gctgggtggc aggttggggc 600
cagaccaatg ctgctgacaa aaactctgtg aaaacggatc tgatgaaagt gccaatggtc 660
atcatggact gggaggagtg ttcaaagatg tttccaaaac ttaccaaaaa tatgctgtgt 720
gccggataca agaatgagag ctatgatgcc tgcaagggtg acagtggggg gcctctggtc 780
tgcaccccag agcctggtga gaagtggtac caggtgggca tcatcagctg gggaaagagc 840
tgtggagaga agaacacccc agggatatac acctcgttgg tgaactacaa cctctggatc 900
gagaaagtga cccagctaga gggcaggccc ttcaatgcag agaaaaggag gacttctgtc 960
aaacagaaac ctatgggctc cccagtctcg ggagtcccag agccaggcag ccccagatcc 1020
tggctcctgc tctgtccccт gtcccatgtg ttgttcagag ctattttgta ctgataataa 1080
aatagaggct attctttca                                              1099
```

<210> 272
<211> 352
<212> PRT
<213> Homo sapiens

<400> 272

```
Met Leu Leu Phe Ser Val Leu Leu Leu Leu Ser Leu Val Thr Gly Thr
```

```
 1               5                  10                  15
Gln Leu Gly Pro Arg Thr Pro Leu Pro Glu Ala Gly Val Ala Ile Leu
            20                  25                  30
Gly Arg Ala Arg Gly Ala His Arg Pro Gln Pro Arg His Pro Pro Ser
        35                  40                  45
Pro Val Ser Glu Cys Gly Asp Arg Ser Ile Phe Glu Gly Arg Thr Arg
    50                  55                  60
Tyr Ser Arg Ile Thr Gly Gly Met Glu Ala Glu Val Gly Glu Phe Pro
65                  70                  75                  80
Trp Gln Val Ser Ile Gln Ala Arg Ser Glu Pro Phe Cys Gly Gly Ser
                85                  90                  95
Ile Leu Asn Lys Trp Trp Ile Leu Thr Ala Ala His Cys Leu Tyr Ser
            100                 105                 110
Glu Glu Leu Phe Pro Glu Glu Leu Ser Val Val Leu Gly Thr Asn Asp
        115                 120                 125
Leu Thr Ser Pro Ser Met Glu Ile Lys Glu Val Ala Ser Ile Ile Leu
    130                 135                 140
His Lys Asp Phe Lys Arg Ala Asn Met Asp Asn Asp Ile Ala Leu Leu
145                 150                 155                 160
Leu Leu Ala Ser Pro Ile Lys Leu Asp Asp Leu Lys Val Pro Ile Cys
                165                 170                 175
Leu Pro Thr Gln Pro Gly Pro Ala Thr Trp Arg Glu Cys Trp Val Ala
            180                 185                 190
Gly Trp Gly Gln Thr Asn Ala Ala Asp Lys Asn Ser Val Lys Thr Asp
        195                 200                 205
Leu Met Lys Val Pro Met Val Ile Met Asp Trp Glu Glu Cys Ser Lys
    210                 215                 220
Met Phe Pro Lys Leu Thr Lys Asn Met Leu Cys Ala Gly Tyr Lys Asn
225                 230                 235                 240
Glu Ser Tyr Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys
                245                 250                 255
Thr Pro Glu Pro Gly Glu Lys Trp Tyr Gln Val Gly Ile Ile Ser Trp
            260                 265                 270
Gly Lys Ser Cys Gly Glu Lys Asn Thr Pro Gly Ile Tyr Thr Ser Leu
        275                 280                 285
Val Asn Tyr Asn Leu Trp Ile Glu Lys Val Thr Gln Leu Glu Gly Arg
    290                 295                 300
Pro Phe Asn Ala Glu Lys Arg Arg Thr Ser Val Lys Gln Lys Pro Met
305                 310                 315                 320
Gly Ser Pro Val Ser Gly Val Pro Glu Pro Gly Ser Pro Arg Ser Trp
                325                 330                 335
Leu Leu Leu Cys Pro Leu Ser His Val Leu Phe Arg Ala Ile Leu Tyr
            340                 345                 350
```

<210> 273
<211> 1927
<212> DNA
<213> Homo sapiens

<400> 273
tgccagccca agtcggaact tggatcacat cagatcctct cgagctccag caggagaggc 60
ccttcctcgc ctggcagccc ctgagcggct cagcagggca ccatggcaag atcccttctc 120
ctgcccctgc agatcttact gctatcctta gccttggaaa ctgcaggaga agaagcccag 180
ggtgacaaga ttattgatgg cgccccatgt gcaagaggct cccacccatg gcaggtggcc 240
ctgctcagtg gcaatcagct ccactgcgga ggcgtcctgg tcaatgagcg ctgggtgctc 300
actgccgccc actgcaagat gaatgagtac accgtgcacc tgggcagtga tacgctgggc 360
gacaggagag ctcagaggat caaggcctcg aagtcattcc gccaccccgg ctactccaca 420

```
cagacccatg ttaatgacct catgctcgtg aagctcaata gccaggccag gctgtcatcc 480
atggtgaaga aagtcaggct gccctcccgc tgcgaacccc ctggaaccac ctgtactgtc 540
tccggctggg gcactaccac gagcccagat gtgacctttc cctctgacct catgtgcgtg 600
gatgtcaagc tcatctcccc ccaggactgc acgaaggttt acaaggactt actggaaaat 660
tccatgctgt gcgctggcat ccccgactcc aagaaaaacg cctgcaatgg tgactcaggg 720
ggaccgttgg tgtgcagagg taccctgcaa ggtctggtgt cctggggaac tttcccttgc 780
ggccaaccca atgacccagg agtctacact caagtgtgca agttcaccaa gtggataaat 840
gacaccatga aaaagcatcg ctaacgccac actgagttaa ttaactgtgt gcttccaaca 900
gaaaatgcac aggagtgagg acgccgatga cctatgaagt caaatttgac tttacctttc 960
ctcaaagata tatttaaacc aacctcatgc cctgttgata aaccaatcaa attggtaaag 1020
acctaaaacc aaaacaaata aagaaacaca aaaccctcag tgctggagaa gagtcagtga 1080
gaccagcact ctcaaacact ggaactggac gttcgtacag tctttacgga agacacttgg 1140
tcaacgtaca ccgagaccct tattcaccac ctttgaccca gtaactctaa tcttaggaag 1200
aacctactga aacaaaaaaa atccaaaatg tagaacaaga cttgaattta ccatgatatt 1260
atttatcaca gaaatgaagt gaaaccatca aacatgttcc aaaagtacca gatggcttaa 1320
ataatagtct ggcttggcac aacgatgttt tttttctttg agacagagtc tctgttgctt 1380
gggctgcaat gcagtgatgc aatcttggct cactgcaacc tccgcctcct gggttcaagt 1440
gattctcgtg cttcagcctc ccaagtacct gggactacag gtgtgcacca ccacaccagg 1500
ctaatttttt gtgtattttt actagagaca gggtttcacc atgttggcca gcgtggtctt 1560
gaacgcctga cctcagatga tccacccacc ttggcctccc aaagtgctgg gattacaggc 1620
atgagccacc acggccagcc cacaatgata ttacaaacct attaaaaatg atacttagac 1680
agaattgtca gtattattca agaacattta ggctatagga tgttaaatga caaaaggaag 1740
gacaaaaata tatatgtatg tgaccctacc cataaaaaat gaaatattca cagaatcaga 1800
tctgaaaaca catgtcccag actgcatact ggggtcgtca tgaggtgtct ccttccttct 1860
gtgtactttt ccttgaatgt gcacttttat aacatgaaaa ataaaggtgg ggaaaaaagt 1920
ctgaaga                                                          1927

<210> 274
<211> 253
<212> PRT
<213> Homo sapiens

<400> 274
Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
 1               5                  10                  15
Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
            20                  25                  30
Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
        35                  40                  45
Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
    50                  55                  60
Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
65                  70                  75                  80
Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
                85                  90                  95
Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
            100                 105                 110
Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
        115                 120                 125
Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
    130                 135                 140
Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
145                 150                 155                 160
Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
                165                 170                 175
Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
            180                 185                 190
Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
```

```
        195                 200                 205
Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe
    210                 215                 220
Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys
225                 230                 235                 240
Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg
                245                 250
```

<210> 275
<211> 1927
<212> DNA
<213> Homo sapiens

<400> 275

```
ggagagggtg atgctggctc caagcctgac tctgctctcg agagctccag caggagaggc 60
ccttcctcgc ctggcagccc ctgagcggct cagcagggca ccatggcaag atcccttctc 120
ctgcccctgc agatcttact gctatcctta gccttggaaa ctgcaggaga agaagcccag 180
ggtgacaaga ttattgatgg cgccccatgt gcaagaggct cccacccatg gcaggtggcc 240
ctgctcagtg gcaatcagct ccactgcgga ggcgtcctgg tcaatgagcg ctgggtgctc 300
actgccgccc actgcaagat gaatgagtac accgtgcacc tgggcagtga tacgctgggc 360
gacaggagag ctcagaggat caaggcctcg aagtcattcc gccaccccgg ctactccaca 420
cagacccatg ttaatgacct catgctcgtg aagctcaata gccaggccag gctgtcatcc 480
atggtgaaga aagtcaggct gccctcccgc tgcgaacccc ctggaaccac ctgtactgtc 540
tccggctggg gcactaccac gagcccagat gtgacctttc cctctgacct catgtgcgtg 600
gatgtcaagc tcatctcccc ccaggactgc acgaaggttt acaaggactt actggaaaat 660
tccatgctgt gcgctggcat ccccgactcc aagaaaaacg cctgcaatgg tgactcaggg 720
ggaccgttgg tgtgcagagg taccctgcaa ggtctggtgt cctggggaac tttcccttgc 780
ggccaaccca atgacccagg agtctacact caagtgtgca agttcaccaa gtggataaat 840
gacaccatga aaaagcatcg ctaacgccac actgagttaa ttaactgtgt gcttccaaca 900
gaaaatgcac aggagtgagg acgccgatga cctatgaagt caaatttgac tttacctttc 960
ctcaaagata tatttaaacc aacctcatgc cctgttgata aaccaatcaa attggtaaag 1020
acctaaaacc aaaacaaata aagaaacaca aaaccctcag tgctggagaa gagtcagtga 1080
gaccagcact ctcaaacact ggaactggac gttcgtacag tctttacgga agacacttgg 1140
tcaacgtaca ccgagaccct tattcaccac ctttgaccca gtaactctaa tcttaggaag 1200
aacctactga aacaaaaaaa atccaaaatg tagaacaaga cttgaattta ccatgatatt 1260
atttatcaca gaaatgaagt gaaaccatca aacatgttcc aaaagtacca gatggcttaa 1320
ataatagtct ggcttggcac aacgatgttt tttttctttg agacagagtc tctgttgctt 1380
gggctgcaat gcagtgatgc aatcttggct cactgcaacc tccgcctcct gggttcaagt 1440
gattctcgtg cttcagcctc ccaagtacct gggactacag gtgtgcacca ccacaccagg 1500
ctaatttttt gtgtatttt actagagaca gggtttcacc atgttggcca gcgtggtctt 1560
gaacgcctga cctcagatga tccacccacc ttggcctccc aaagtgctgg gattacaggc 1620
atgagccacc acggccagcc cacaatgata ttacaaacct attaaaaatg atacttagac 1680
agaattgtca gtattattca agaacattta ggctatagga tgttaaatga caaaaggaag 1740
gacaaaaata tatatgtatg tgaccctacc cataaaaaat gaaatattca cagaatcaga 1800
tctgaaaaca catgtcccag actgcatact ggggtcgtca tgaggtgtct ccttccttct 1860
gtgtactttt ccttgaatgt gcacttttat aacatgaaaa ataaaggtgg ggaaaaaagt 1920
ctgaaga                                                          1927
```

<210> 276
<211> 253
<212> PRT
<213> Homo sapiens

<400> 276

```
Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
 1               5                  10                  15
Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
```

```
            20                  25                  30
Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
        35                  40                  45
Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
    50                  55                  60
Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
65                  70                  75                  80
Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
                85                  90                  95
Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
            100                 105                 110
Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
        115                 120                 125
Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
    130                 135                 140
Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
145                 150                 155                 160
Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
                165                 170                 175
Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
            180                 185                 190
Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
        195                 200                 205
Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe
    210                 215                 220
Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys
225                 230                 235                 240
Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg
                245                 250
```

<210> 277
<211> 2800
<212> DNA
<213> Homo sapiens

<400> 277

```
atttgagtgg gaatctcaaa gcagttgagt aggcagaaaa aagaacctct tcattaagga 60
ttaaaatgta taggccagca cgtgtaactt cgacttcaag atttctgaat ccatatgtag 120
tatgtttcat tgtcgtcgca ggggtagtga tcctggcagt caccatagct ctacttgttt 180
acttttagc ttttgatcaa aaatcttact tttataggag cagttttcaa ctcctaaatg 240
ttgaatataa tagtcagtta aattcaccag ctacacagga atacaggact ttgagtggaa 300
gaattgaatc tctgattact aaaacattca aagaatcaaa tttaagaaat cagttcatca 360
gagctcatgt tgccaaactg aggcaagatg gtagtggtgt gagagcggat gttgtcatga 420
aatttcaatt cactagaaat aacaatggag catcaatgaa aagcagaatt gagtctgttt 480
tacgacaaat gctgaataac tctggaaacc tggaaataaa cccttcaact gagataacat 540
cacttactga ccaggctgca gcaaattggc ttattaatga atgtggggcc ggtccagacc 600
taataacatt gtctgagcag agaatccttg gaggcactga ggctgaggag ggaagctggc 660
cgtggcaagt cagtctgcgg ctcaataatg cccaccactg tggaggcagc ctgatcaata 720
acatgtggat cctgacagca gctcactgct tcagaagcaa ctctaatcct cgtgactgga 780
ttgccacgtc tggtatttcc acaacatttc ctaaactaag aatgagagta agaaatattt 840
taattcataa caattataaa tctgcaactc atgaaaatga cattgcactt gtgagacttg 900
agaacagtgt caccttacc aaagatatcc atagtgtgtg tctcccagct gctacccaga 960
atattccacc tggctctact gcttatgtaa caggatgggg cgctcaagaa tatgctggcc 1020
acacagttcc agagctaagg caaggacagg tcagaataat aagtaatgat gtatgtaatg 1080
caccacatag ttataatgga gccatcttgt ctggaatgct gtgtgctgga gtacctcaag 1140
gtggagtgga cgcatgtcag ggtgactctg gtggcccact agtacaagaa gactcacggc 1200
ggctttggtt tattgtgggg atagtaagct ggggagatca gtgtggcctg ccggataagc 1260
```

caggagtgta tactcgagtg acagcctacc ttgactggat taggcaacaa actgggatct 1320
agtgcaacaa gtgcatccct gttgcaaagt ctgtatgcag gtgtgcctgt cttaaattcc 1380
aaagctttac atttcaactg aaaaagaaac tagaaatgtc ctaatttaac atcttgttac 1440
ataaatatgg tttaacaaac actgtttaac ctttctttat tattaaaggt tttctatttt 1500
ctccagagaa ctatatgaat gttgcatagt actgtggctg tgtaacagaa gaaacacact 1560
aaactaatta caaagttaac aatttcatta cagttgtgct aaatgcccgt agtgagaaga 1620
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<210> 278
<211> 418
<212> PRT
<213> Homo sapiens

<400> 278

Met	Tyr	Arg	Pro	Ala	Arg	Val	Thr	Ser	Thr	Ser	Arg	Phe	Leu	Asn	Pro
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Tyr	Val	Val	Cys	Phe	Ile	Val	Val	Ala	Gly	Val	Val	Ile	Leu	Ala	Val
			20					25				30			
Thr	Ile	Ala	Leu	Leu	Val	Tyr	Phe	Leu	Ala	Phe	Asp	Gln	Lys	Ser	Tyr
		35					40					45			
Phe	Tyr	Arg	Ser	Ser	Phe	Gln	Leu	Leu	Asn	Val	Glu	Tyr	Asn	Ser	Gln
	50					55					60				
Leu	Asn	Ser	Pro	Ala	Thr	Gln	Glu	Tyr	Arg	Thr	Leu	Ser	Gly	Arg	Ile
65					70					75					80
Glu	Ser	Leu	Ile	Thr	Lys	Thr	Phe	Lys	Glu	Ser	Asn	Leu	Arg	Asn	Gln
				85					90					95	
Phe	Ile	Arg	Ala	His	Val	Ala	Lys	Leu	Arg	Gln	Asp	Gly	Ser	Gly	Val
			100					105					110		
Arg	Ala	Asp	Val	Val	Met	Lys	Phe	Gln	Phe	Thr	Arg	Asn	Asn	Asn	Gly
		115					120					125			
Ala	Ser	Met	Lys	Ser	Arg	Ile	Glu	Ser	Val	Leu	Arg	Gln	Met	Leu	Asn
	130					135					140				
Asn	Ser	Gly	Asn	Leu	Glu	Ile	Asn	Pro	Ser	Thr	Glu	Ile	Thr	Ser	Leu
145					150					155					160
Thr	Asp	Gln	Ala	Ala	Ala	Asn	Trp	Leu	Ile	Asn	Glu	Cys	Gly	Ala	Gly
				165					170					175	
Pro	Asp	Leu	Ile	Thr	Leu	Ser	Glu	Gln	Arg	Ile	Leu	Gly	Gly	Thr	Glu
			180					185					190		
Ala	Glu	Glu	Gly	Ser	Trp	Pro	Trp	Gln	Val	Ser	Leu	Arg	Leu	Asn	Asn

```
        195                 200                 205
Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
    210                 215                 220
Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
225                 230                 235                 240
Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
                245                 250                 255
Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
            260                 265                 270
Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
        275                 280                 285
His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
    290                 295                 300
Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
305                 310                 315                 320
Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
                325                 330                 335
Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
            340                 345                 350
Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
        355                 360                 365
Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
    370                 375                 380
Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
385                 390                 395                 400
Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr
                405                 410                 415
Gly Ile
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<210> 279
<211> 1258
<212> DNA
<213> Homo sapiens

<400> 279

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tctcaacacc aatgggacca gtgggtttct cccaggtggc tacacctgct tcccccactc 180
tcagccctgg caggctgccc tactagtgca agggcggcta ctctgtgggg gagtcctggt 240
ccaccccaaa tgggtcctca ctgccgcaca ctgtctaaag gaggggctca aagtttacct 300
aggcaagcac gccctagggc gtgtggaagc tggtgagcag gtgagggaag ttgtccactc 360
tatcccccac cctgaatacc ggagaagccc cacccacctg aaccacgacc atgacatcat 420
gcttctggag ctgcagtccc cggtccagct cacaggctac atccaaaccc tgccccttc 480
ccacaacaac cgcctaaccc ctggcaccac ctgtcgggtg tctggctggg gcaccaccac 540
cagccccag gtgaattacc ccaaaactct acaatgtgcc aacatccaac ttcgctcaga 600
tgaggagtgt cgtcaagtct acccaggaaa gatcactgac aacatgttgt gtgccggcac 660
aaaagagggt ggcaaagact cctgtgaggg tgactctggg ggccccctgg tctgtaacag 720
aacactgtat ggcatcgtct cctggggaga cttcccatgt gggcaacctg accggcctgg 780
tgtctacacc cgtgtctcaa gatacgtcct gtggatccgt gaaacaatcc gaaaatatga 840
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catcctgtca ccatgacttc ctcacatggt ctgcttagcc cttctctgct ccttattccc 960
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cagtgtggct tctatgagcc cagatcacca cctgaacgtt ctgtctgtgg cacattctta 1200
aatatttcca tcagcccatc tcaacaatat atgtcctata aatggaccat ccttgaca   1258
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<210> 280
<211> 277
<212> PRT
<213> Homo sapiens

<400> 280
Met Trp Pro Leu Ala Leu Val Ile Ala Ser Leu Thr Leu Ala Leu Ser
1 5 10 15
Gly Gly Val Ser Gln Glu Ser Ser Lys Val Leu Asn Thr Asn Gly Thr
20 25 30
Ser Gly Phe Leu Pro Gly Gly Tyr Thr Cys Phe Pro His Ser Gln Pro
35 40 45
Trp Gln Ala Ala Leu Leu Val Gln Gly Arg Leu Leu Cys Gly Gly Val
50 55 60
Leu Val His Pro Lys Trp Val Leu Thr Ala Ala His Cys Leu Lys Glu
65 70 75 80
Gly Leu Lys Val Tyr Leu Gly Lys His Ala Leu Gly Arg Val Glu Ala
85 90 95
Gly Glu Gln Val Arg Glu Val Val His Ser Ile Pro His Pro Glu Tyr
100 105 110
Arg Arg Ser Pro Thr His Leu Asn His Asp His Asp Ile Met Leu Leu
115 120 125
Glu Leu Gln Ser Pro Val Gln Leu Thr Gly Tyr Ile Gln Thr Leu Pro
130 135 140
Leu Ser His Asn Asn Arg Leu Thr Pro Gly Thr Thr Cys Arg Val Ser
145 150 155 160
Gly Trp Gly Thr Thr Thr Ser Pro Gln Val Asn Tyr Pro Lys Thr Leu
165 170 175
Gln Cys Ala Asn Ile Gln Leu Arg Ser Asp Glu Glu Cys Arg Gln Val
180 185 190
Tyr Pro Gly Lys Ile Thr Asp Asn Met Leu Cys Ala Gly Thr Lys Glu
195 200 205
Gly Gly Lys Asp Ser Cys Glu Gly Asp Ser Gly Gly Pro Leu Val Cys
210 215 220
Asn Arg Thr Leu Tyr Gly Ile Val Ser Trp Gly Asp Phe Pro Cys Gly
225 230 235 240
Gln Pro Asp Arg Pro Gly Val Tyr Thr Arg Val Ser Arg Tyr Val Leu
245 250 255
Trp Ile Arg Glu Thr Ile Arg Lys Tyr Glu Thr Gln Gln Gln Lys Trp
260 265 270
Leu Lys Gly Pro Gln
275

<210> 281
<211> 1438
<212> DNA
<213> Homo sapiens

<400> 281
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gttccaggat ccaggtgccc aggggtcatg aagctgggac tcctctgtgc tctgctctct 120
ctgctggcag ggcatggctg ggcagacacc cgtgccatcg gggccgagga atgtcgcccc 180
aactcccagc cttggcaggc cggcctcttc caccttactc ggctcttctg tggggcgacc 240
ctcatcagtg accgctggct gctcacagct gcccactgcc gcaagccgta tctgtgggtc 300
cgccttggag agcaccacct ctggaaatgg gagggtccgg agcagctgtt ccgggttacg 360
gacttcttcc cccaccctgg cttcaacaag gacctcagcg ccaatgacca caatgatgac 420

atcatgctga tccgcctgcc caggcaggca cgtctgagtc ctgctgtgca gcccctcaac 480
ctcagccaga cctgtgtctc cccaggcatg cagtgtctca tctcaggctg gggggccgtg 540
tccagcccca aggcgctgtt tccagtcaca ctgcagtgtg ccaacatcag catcctggag 600
aacaaactct gtcactgggc ataccctgga cacatctcgg acagcatgct ctgtgcgggc 660
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ggaaccttgg caggcgtggt gtctgggggt gctgagccct gctccagacc ccggcgcccc 780
gcagtctaca ccagcgtatg ccactacctt gactggatcc aagaaatcat ggagaactga 840
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tcaccgacag ccatcacctc cttcttggaa cagcacagcc tgtggctccg ccccaaggaa 1140
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<210> 282
<211> 250
<212> PRT
<213> Homo sapiens

<400> 282

Met	Lys	Leu	Gly	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Leu	Leu	Ala	Gly	His
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Gly	Trp	Ala	Asp	Thr	Arg	Ala	Ile	Gly	Ala	Glu	Glu	Cys	Arg	Pro	Asn
			20					25					30		
Ser	Gln	Pro	Trp	Gln	Ala	Gly	Leu	Phe	His	Leu	Thr	Arg	Leu	Phe	Cys
		35					40					45			
Gly	Ala	Thr	Leu	Ile	Ser	Asp	Arg	Trp	Leu	Leu	Thr	Ala	Ala	His	Cys
	50					55					60				
Arg	Lys	Pro	Tyr	Leu	Trp	Val	Arg	Leu	Gly	Glu	His	His	Leu	Trp	Lys
65					70					75					80
Trp	Glu	Gly	Pro	Glu	Gln	Leu	Phe	Arg	Val	Thr	Asp	Phe	Phe	Pro	His
				85					90					95	
Pro	Gly	Phe	Asn	Lys	Asp	Leu	Ser	Ala	Asn	Asp	His	Asn	Asp	Asp	Ile
			100					105					110		
Met	Leu	Ile	Arg	Leu	Pro	Arg	Gln	Ala	Arg	Leu	Ser	Pro	Ala	Val	Gln
		115					120					125			
Pro	Leu	Asn	Leu	Ser	Gln	Thr	Cys	Val	Ser	Pro	Gly	Met	Gln	Cys	Leu
	130					135					140				
Ile	Ser	Gly	Trp	Gly	Ala	Val	Ser	Ser	Pro	Lys	Ala	Leu	Phe	Pro	Val
145					150					155					160
Thr	Leu	Gln	Cys	Ala	Asn	Ile	Ser	Ile	Leu	Glu	Asn	Lys	Leu	Cys	His
				165					170					175	
Trp	Ala	Tyr	Pro	Gly	His	Ile	Ser	Asp	Ser	Met	Leu	Cys	Ala	Gly	Leu
			180					185					190		
Trp	Glu	Gly	Gly	Arg	Gly	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu
		195					200					205			
Val	Cys	Asn	Gly	Thr	Leu	Ala	Gly	Val	Val	Ser	Gly	Gly	Ala	Glu	Pro
	210					215					220				
Cys	Ser	Arg	Pro	Arg	Arg	Pro	Ala	Val	Tyr	Thr	Ser	Val	Cys	His	Tyr
225					230					235					240
Leu	Asp	Trp	Ile	Gln	Glu	Ile	Met	Glu	Asn						
				245					250						

<210> 283
<211> 3212
<212> DNA
<213> Homo sapiens

<400> 283
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ttactcttcc actccaaaag gatgcccgtg gccgaggccc cccaggtggc tggcgggcag 180
ggggacggag gtgatggcga ggaagcggag ccggagggga tgttcaaggc ctgtgaggac 240
tccaagagaa aagcccgggg ctacctccgc ctggtgcccc tgtttgtgct gctggccctg 300
ctcgtgctgg cttcggcggg ggtgctactc tggtatttcc tagggtacaa ggcggaggtg 360
atggtcagcc aggtgtactc aggcagtctg cgtgtactca atcgccactt ctcccaggat 420
cttacccgcc gggaatctag tgccttccgc agtgaaaccg ccaaagccca gaagatgctc 480
aaggagctca tcaccagcac ccgcctggga acttactaca actccagctc cgtctattcc 540
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cggctgatgc tgagccccga ggtggtgcag gcactgctgg tggaggagct gctgtccaca 660
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ctgggccctc acagcccaga ccctcactgg gaggtgagct cagctgccct ttggaataaa 3180
gctgcctgat caaaaaaaaa aaaaaaaaaa aa 3212

<210> 284
<211> 811
<212> PRT
<213> Homo sapiens

<400> 284

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Gln Val Ala Gly Gly Gln Gly Asp Gly Gly Asp Gly Glu Glu Ala Glu
            20                  25                  30
Pro Glu Gly Met Phe Lys Ala Cys Glu Asp Ser Lys Arg Lys Ala Arg
        35                  40                  45
Gly Tyr Leu Arg Leu Val Pro Leu Phe Val Leu Leu Ala Leu Leu Val
    50                  55                  60
Leu Ala Ser Ala Gly Val Leu Leu Trp Tyr Phe Leu Gly Tyr Lys Ala
65                  70                  75                  80
Glu Val Met Val Ser Gln Val Tyr Ser Gly Ser Leu Arg Val Leu Asn
                85                  90                  95
Arg His Phe Ser Gln Asp Leu Thr Arg Arg Glu Ser Ser Ala Phe Arg
            100                 105                 110
Ser Glu Thr Ala Lys Ala Gln Lys Met Leu Lys Glu Leu Ile Thr Ser
        115                 120                 125
Thr Arg Leu Gly Thr Tyr Tyr Asn Ser Ser Ser Val Tyr Ser Phe Gly
    130                 135                 140
Glu Gly Pro Leu Thr Cys Phe Phe Trp Phe Ile Leu Gln Ile Pro Glu
145                 150                 155                 160
His Arg Arg Leu Met Leu Ser Pro Glu Val Val Gln Ala Leu Leu Val
                165                 170                 175
Glu Glu Leu Leu Ser Thr Val Asn Ser Ser Ala Ala Val Pro Tyr Arg
            180                 185                 190
Ala Glu Tyr Glu Val Asp Pro Glu Gly Leu Val Ile Leu Glu Ala Ser
        195                 200                 205
Val Lys Asp Ile Ala Ala Leu Asn Ser Thr Leu Gly Cys Tyr Arg Tyr
    210                 215                 220
Ser Tyr Val Gly Gln Gly Gln Val Leu Arg Leu Lys Gly Pro Asp His
225                 230                 235                 240
Leu Ala Ser Ser Cys Leu Trp His Leu Gln Gly Pro Lys Asp Leu Met
                245                 250                 255
Leu Lys Leu Arg Leu Glu Trp Thr Leu Ala Glu Cys Arg Asp Arg Leu
            260                 265                 270
Ala Met Tyr Asp Val Ala Gly Pro Leu Glu Lys Arg Leu Ile Thr Ser
        275                 280                 285
Val Tyr Gly Cys Ser Arg Gln Glu Pro Val Val Glu Val Leu Ala Ser
    290                 295                 300
Gly Ala Ile Met Ala Val Val Trp Lys Lys Gly Leu His Ser Tyr Tyr
305                 310                 315                 320
Asp Pro Phe Val Leu Ser Val Gln Pro Val Val Phe Gln Ala Cys Glu
                325                 330                 335
Val Asn Leu Thr Leu Asp Asn Arg Leu Asp Ser Gln Gly Val Leu Ser
            340                 345                 350
Thr Pro Tyr Phe Pro Ser Tyr Tyr Ser Pro Gln Thr His Cys Ser Trp
        355                 360                 365
His Leu Thr Val Pro Ser Leu Asp Tyr Gly Leu Ala Leu Trp Phe Asp
    370                 375                 380
Ala Tyr Ala Leu Arg Arg Gln Lys Tyr Asp Leu Pro Cys Thr Gln Gly
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385 390 395 400
Gln Trp Thr Ile Gln Asn Arg Arg Leu Cys Gly Leu Arg Ile Leu Gln
405 410 415
Pro Tyr Ala Glu Arg Ile Pro Val Val Ala Thr Ala Gly Ile Thr Ile
420 425 430
Asn Phe Thr Ser Gln Ile Ser Leu Thr Gly Pro Gly Val Arg Val His
435 440 445
Tyr Gly Leu Tyr Asn Gln Ser Asp Pro Cys Pro Gly Glu Phe Leu Cys
450 455 460
Ser Val Asn Gly Leu Cys Val Pro Ala Cys Asp Gly Val Lys Asp Cys
465 470 475 480
Pro Asn Gly Leu Asp Glu Arg Asn Cys Val Cys Arg Ala Thr Phe Gln
485 490 495
Cys Lys Glu Asp Ser Thr Cys Ile Ser Leu Pro Lys Val Cys Asp Gly
500 505 510
Gln Pro Asp Cys Leu Asn Gly Ser Asp Glu Glu Gln Cys Gln Glu Gly
515 520 525
Val Pro Cys Gly Thr Phe Thr Phe Gln Cys Glu Asp Arg Ser Cys Val
530 535 540
Lys Lys Pro Asn Pro Gln Cys Asp Gly Arg Pro Asp Cys Arg Asp Gly
545 550 555 560
Ser Asp Glu Glu His Cys Asp Cys Gly Leu Gln Gly Pro Ser Ser Arg
565 570 575
Ile Val Gly Gly Ala Val Ser Ser Glu Gly Glu Trp Pro Trp Gln Ala
580 585 590
Ser Leu Gln Val Arg Gly Arg His Ile Cys Gly Gly Ala Leu Ile Ala
595 600 605
Asp Arg Trp Val Ile Thr Ala Ala His Cys Phe Gln Glu Asp Ser Met
610 615 620
Ala Ser Thr Val Leu Trp Thr Val Phe Leu Gly Lys Val Trp Gln Asn
625 630 635 640
Ser Arg Trp Pro Gly Glu Val Ser Phe Lys Val Ser Arg Leu Leu Leu
645 650 655
His Pro Tyr His Glu Glu Asp Ser His Asp Tyr Asp Val Ala Leu Leu
660 665 670
Gln Leu Asp His Pro Val Val Arg Ser Ala Ala Val Arg Pro Val Cys
675 680 685
Leu Pro Ala Arg Ser His Phe Phe Glu Pro Gly Leu His Cys Trp Ile
690 695 700
Thr Gly Trp Gly Ala Leu Arg Glu Gly Gly Pro Ile Ser Asn Ala Leu
705 710 715 720
Gln Lys Val Asp Val Gln Leu Ile Pro Gln Asp Leu Cys Ser Glu Val
725 730 735
Tyr Arg Tyr Gln Val Thr Pro Arg Met Leu Cys Ala Gly Tyr Arg Lys
740 745 750
Gly Lys Lys Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
755 760 765
Lys Ala Leu Ser Gly Arg Trp Phe Leu Ala Gly Leu Val Ser Trp Gly
770 775 780
Leu Gly Cys Gly Arg Pro Asn Tyr Phe Gly Val Tyr Thr Arg Ile Thr
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Gly Val Ile Ser Trp Ile Gln Gln Val Val Thr
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<210> 285
<211> 3750
<212> DNA

<213> Homo sapiens

<400> 285

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<210> 286
<211> 383
<212> PRT
<213> Homo sapiens

<400> 286

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Ala	Val	Gly	Gln	Val	Ser	Pro	Tyr	Ser	Ala	Pro	Trp	Lys	Pro	Thr	Trp
			20					25				30			
Pro	Ala	Tyr	Arg	Leu	Pro	Val	Val	Leu	Pro	Gln	Ser	Thr	Leu	Asn	Leu
		35					40					45			
Ala	Lys	Pro	Asp	Phe	Gly	Ala	Glu	Ala	Lys	Leu	Glu	Val	Ser	Ser	Ser
	50					55					60				
Cys	Gly	Pro	Gln	Cys	His	Lys	Gly	Thr	Pro	Leu	Pro	Thr	Tyr	Glu	Glu
65					70					75					80
Ala	Lys	Gln	Tyr	Leu	Ser	Tyr	Glu	Thr	Leu	Tyr	Ala	Asn	Gly	Ser	Arg
				85					90					95	
Thr	Glu	Thr	Gln	Val	Gly	Ile	Tyr	Ile	Leu	Ser	Ser	Ser	Gly	Asp	Gly
			100					105					110		
Ala	Gln	His	Arg	Asp	Ser	Gly	Ser	Ser	Gly	Lys	Ser	Arg	Arg	Lys	Arg
		115					120					125			
Gln	Ile	Tyr	Gly	Tyr	Asp	Ser	Arg	Phe	Ser	Ile	Phe	Gly	Lys	Asp	Phe
	130					135					140				
Leu	Leu	Asn	Tyr	Pro	Phe	Ser	Thr	Ser	Val	Lys	Leu	Ser	Thr	Gly	Cys
145					150					155					160
Thr	Gly	Thr	Leu	Val	Ala	Glu	Lys	His	Val	Leu	Thr	Ala	Ala	His	Cys
				165					170					175	
Ile	His	Asp	Gly	Lys	Thr	Tyr	Val	Lys	Gly	Thr	Gln	Lys	Leu	Arg	Val
			180					185					190		
Gly	Phe	Leu	Lys	Pro	Lys	Phe	Lys	Asp	Gly	Gly	Arg	Gly	Ala	Asn	Asp
		195					200					205			
Ser	Thr	Ser	Ala	Met	Pro	Glu	Gln	Met	Lys	Phe	Gln	Trp	Ile	Arg	Val
	210					215					220				
Lys	Arg	Thr	His	Val	Pro	Lys	Gly	Trp	Ile	Lys	Gly	Asn	Ala	Asn	Asp
225					230					235					240
Ile	Gly	Met	Asp	Tyr	Asp	Tyr	Ala	Leu	Leu	Glu	Leu	Lys	Lys	Pro	His
				245					250					255	
Lys	Arg	Lys	Phe	Met	Lys	Ile	Gly	Val	Ser	Pro	Pro	Ala	Lys	Gln	Leu
			260					265					270		
Pro	Gly	Gly	Arg	Ile	His	Phe	Ser	Gly	Tyr	Asp	Asn	Asp	Arg	Pro	Gly
		275					280					285			
Asn	Leu	Val	Tyr	Arg	Phe	Cys	Asp	Val	Lys	Asp	Glu	Thr	Tyr	Asp	Leu
	290					295					300				
Leu	Tyr	Gln	Gln	Cys	Asp	Ala	Gln	Pro	Gly	Ala	Ser	Gly	Ser	Gly	Val
305					310					315					320
Tyr	Val	Arg	Met	Trp	Lys	Arg	Gln	Gln	Gln	Lys	Trp	Glu	Arg	Lys	Ile
				325					330					335	
Ile	Gly	Ile	Phe	Ser	Gly	His	Gln	Trp	Val	Asp	Met	Asn	Gly	Ser	Pro

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            340                 345                 350
Gln Asp Phe Asn Val Ala Val Arg Ile Thr Pro Leu Lys Tyr Ala Gln
        355                 360                 365
Ile Cys Tyr Trp Ile Lys Gly Asn Tyr Leu Asp Cys Arg Glu Gly
    370                 375                 380
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<210> 287
<211> 26
<212> PRT
<213> Homo sapiens

<400> 287

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Ile Ile Gly Gly Thr Glu Ser Lys Pro Asp Ser Arg Pro Tyr Met Ala
 1               5                  10                  15
Leu Leu Gln Ile Val Glu Pro Ala Val His
            20                  25
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<210> 288
<211> 2265
<212> DNA
<213> Homo sapiens

<400> 288

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gaccctgagg ctttacaaca gtgctactga cccctatgag cctgatgctg gatgaccaac 180
cccctatgga ggcccagtat gcagaggagg gcccaggacc tgggatcttc agagcagagc 240
ctggagacca gcagcatccc atttctcagg cggtgtgctg gcgttccatg cgacgtggct 300
gtgcagtgct gggagccctg gggctgctgg ccggtgcagg tgttggctca tggctcctag 360
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cagtatcttt cagaataaac agcgaagact tcttgctgga agcgcaagtg agggatcagc 540
cacgctggct cctggtctgc catgagggct ggagccccgc cctggggctg cagatctgct 600
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tcaacagttc ccaggagttt gctcagctct ctcctagact gggaggcttc ctggaggagg 720
cgtggcagcc caggaacaac tgcacttctg gtcaagttgt ttccctcaga tgctctgagt 780
gtggagcgag gcccctggct tcccggatag ttggtgggca gtctgtggct cctgggcgct 840
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gaagcctgcc cttctgccct ctcccctccc tgcccctgtg tgagtctttt agggagggtg 1920
actgggaggt gccccccgtc ccacctttct cctgtgctct aggtgggcta agtgcctccc 1980
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tagaggactc catggctgag aggctcctgg gcagatgggg tcaaggctgg gccagtccca 2040
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<210> 289
<211> 457
<212> PRT
<213> Homo sapiens

<400> 289

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Glu	Glu	Gly	Pro	Gly	Pro	Gly	Ile	Phe	Arg	Ala	Glu	Pro	Gly	Asp	Gln
			20					25				30			
Gln	His	Pro	Ile	Ser	Gln	Ala	Val	Cys	Trp	Arg	Ser	Met	Arg	Arg	Gly
		35					40					45			
Cys	Ala	Val	Leu	Gly	Ala	Leu	Gly	Leu	Leu	Ala	Gly	Ala	Gly	Val	Gly
	50					55					60				
Ser	Trp	Leu	Leu	Val	Leu	Tyr	Leu	Cys	Pro	Ala	Ala	Ser	Gln	Pro	Ile
65					70					75					80
Ser	Gly	Thr	Leu	Gln	Asp	Glu	Glu	Ile	Thr	Leu	Ser	Cys	Ser	Glu	Ala
				85					90					95	
Ser	Ala	Glu	Glu	Ala	Leu	Leu	Pro	Ala	Leu	Pro	Lys	Thr	Val	Ser	Phe
			100					105					110		
Arg	Ile	Asn	Ser	Glu	Asp	Phe	Leu	Leu	Glu	Ala	Gln	Val	Arg	Asp	Gln
		115					120					125			
Pro	Arg	Trp	Leu	Leu	Val	Cys	His	Glu	Gly	Trp	Ser	Pro	Ala	Leu	Gly
	130					135					140				
Leu	Gln	Ile	Cys	Trp	Ser	Leu	Gly	His	Leu	Arg	Leu	Thr	His	His	Lys
145					150					155					160
Gly	Val	Asn	Leu	Thr	Asp	Ile	Lys	Leu	Asn	Ser	Ser	Gln	Glu	Phe	Ala
				165					170					175	
Gln	Leu	Ser	Pro	Arg	Leu	Gly	Gly	Phe	Leu	Glu	Glu	Ala	Trp	Gln	Pro
			180					185					190		
Arg	Asn	Asn	Cys	Thr	Ser	Gly	Gln	Val	Val	Ser	Leu	Arg	Cys	Ser	Glu
		195					200					205			
Cys	Gly	Ala	Arg	Pro	Leu	Ala	Ser	Arg	Ile	Val	Gly	Gly	Gln	Ser	Val
	210					215					220				
Ala	Pro	Gly	Arg	Trp	Pro	Trp	Gln	Ala	Ser	Val	Ala	Leu	Gly	Phe	Arg
225					230					235					240
His	Thr	Cys	Gly	Gly	Ser	Val	Leu	Ala	Pro	Arg	Trp	Val	Val	Thr	Ala
				245					250					255	
Ala	His	Cys	Met	His	Ser	Phe	Arg	Leu	Ala	Arg	Leu	Ser	Ser	Trp	Arg
			260					265					270		
Val	His	Ala	Gly	Leu	Val	Ser	His	Ser	Ala	Val	Arg	Pro	His	Gln	Gly
		275					280					285			
Ala	Leu	Val	Glu	Arg	Ile	Ile	Pro	His	Pro	Leu	Tyr	Ser	Ala	Gln	Asn
	290					295					300				
His	Asp	Tyr	Asp	Val	Ala	Leu	Leu	Arg	Leu	Gln	Thr	Ala	Leu	Asn	Phe
305					310					315					320
Ser	Asp	Thr	Val	Gly	Ala	Val	Cys	Leu	Pro	Ala	Lys	Glu	Gln	His	Phe
				325					330					335	
Pro	Lys	Gly	Ser	Arg	Cys	Trp	Val	Ser	Gly	Trp	Gly	His	Thr	His	Pro
			340					345					350		
Ser	His	Thr	Tyr	Ser	Ser	Asp	Met	Leu	Gln	Asp	Thr	Val	Val	Pro	Leu
		355					360					365			

```
Phe Ser Thr Gln Leu Cys Asn Ser Ser Cys Val Tyr Ser Gly Ala Leu
    370                 375                 380
Thr Pro Arg Met Leu Cys Ala Gly Tyr Leu Asp Gly Arg Ala Asp Ala
385                 390                 395                 400
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Pro Asp Gly Asp Thr
                405                 410                 415
Trp Arg Leu Val Gly Val Val Ser Trp Gly Arg Ala Cys Ala Glu Pro
            420                 425                 430
Asn His Pro Gly Val Tyr Ala Lys Val Ala Glu Phe Leu Asp Trp Ile
        435                 440                 445
His Asp Thr Ala Gln Asp Ser Leu Leu
    450                 455
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<210> 290
<211> 1243
<212> DNA
<213> Homo sapiens

<400> 290
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cagggaatct ccctaactgg cagcgtggcc tgtggtcggc ccagcatgga ggggaaaatc 180
ctgggcggcg tccctgcgcc cgagaggaag tggccgtggc aggtcagcgt gcactacgca 240
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tgctttcaca gggacaagaa tatcaaaatc tatgacatgt acgtaggcct cgtaaacctc 360
agggtggccg gcaaccacac ccagtggtat gaggtgaaca gggtgatcct gcaccccaca 420
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gtgttttctg agtccgtgct cccggtttgc cttgcaactc cagaagtgaa ccttaccagt 540
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tgtgagggcg actccggggg cccacttgtc tgtgaattca accgcagctg gttgcagatt 780
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cagacaaggg ccacctatcc cgggggtgga tgctgagtcc aggaggtgat gagcaagtgt 1140
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tgcacctgag atttgataag atcattaaat atttacaaag caa 1243

<210> 291
<211> 326
<212> PRT
<213> Homo sapiens

<400> 291
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Gly Leu Leu Leu Leu Leu Leu Val Val Ala Pro Pro Arg Val Ala Ala
            20                  25                  30
Leu Val His Arg Gln Pro Glu Asn Gln Gly Ile Ser Leu Thr Gly Ser
        35                  40                  45
Val Ala Cys Gly Arg Pro Ser Met Glu Gly Lys Ile Leu Gly Gly Val
    50                  55                  60
Pro Ala Pro Glu Arg Lys Trp Pro Trp Gln Val Ser Val His Tyr Ala
65                  70                  75                  80
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Gly Leu His Val Cys Gly Gly Ser Ile Leu Asn Glu Tyr Trp Val Leu
                85                  90                  95
Ser Ala Ala His Cys Phe His Arg Asp Lys Asn Ile Lys Ile Tyr Asp
            100                 105                 110
Met Tyr Val Gly Leu Val Asn Leu Arg Val Ala Gly Asn His Thr Gln
        115                 120                 125
Trp Tyr Glu Val Asn Arg Val Ile Leu His Pro Thr Tyr Glu Met Tyr
    130                 135                 140
His Pro Ile Gly Gly Asp Val Ala Leu Val Gln Leu Lys Thr Arg Ile
145                 150                 155                 160
Val Phe Ser Glu Ser Val Leu Pro Val Cys Leu Ala Thr Pro Glu Val
                165                 170                 175
Asn Leu Thr Ser Ala Asn Cys Trp Ala Thr Gly Trp Gly Leu Val Ser
            180                 185                 190
Lys Gln Gly Glu Thr Ser Asp Glu Leu Gln Glu Met Gln Leu Pro Leu
        195                 200                 205
Ile Leu Glu Pro Trp Cys His Leu Leu Tyr Gly His Met Ser Tyr Ile
    210                 215                 220
Met Pro Asp Met Leu Cys Ala Gly Asp Ile Leu Asn Ala Lys Thr Val
225                 230                 235                 240
Cys Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Glu Phe Asn Arg Ser
                245                 250                 255
Trp Leu Gln Ile Gly Ile Val Ser Trp Gly Arg Gly Cys Ser Asn Pro
            260                 265                 270
Leu Tyr Pro Gly Val Tyr Ala Ser Val Ser Tyr Phe Ser Lys Trp Ile
        275                 280                 285
Cys Asp Asn Ile Glu Ile Thr Pro Thr Pro Ala Gln Pro Ala Pro Ala
    290                 295                 300
Leu Ser Pro Ala Leu Gly Pro Thr Leu Ser Val Leu Met Ala Met Leu
305                 310                 315                 320
Ala Gly Trp Ser Val Leu
                325
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<210> 292
<211> 1695
<212> DNA
<213> Homo sapiens

<400> 292

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<210> 293
<211> 564
<212> PRT
<213> Homo sapiens

<400> 293

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Cys Gly Gln Ser Leu Val Lys Val Gln Pro Trp Asn Tyr Phe Asn Ile
        35                  40                  45
Phe Ser Arg Ile Leu Gly Gly Ser Gln Val Glu Lys Gly Ser Tyr Pro
    50                  55                  60
Trp Gln Val Ser Leu Lys Gln Arg Gln Lys His Ile Cys Gly Gly Ser
65                  70                  75                  80
Ile Val Ser Pro Gln Trp Val Ile Thr Ala Ala His Cys Ile Ala Asn
                85                  90                  95
Arg Asn Ile Val Ser Thr Leu Asn Val Thr Ala Gly Glu Tyr Asp Leu
            100                 105                 110
Ser Gln Thr Asp Pro Gly Glu Gln Thr Leu Thr Ile Glu Thr Val Ile
        115                 120                 125
Ile His Pro His Phe Ser Thr Lys Lys Pro Met Asp Tyr Asp Ile Ala
    130                 135                 140
Leu Leu Lys Met Ala Gly Ala Phe Gln Phe Gly His Phe Val Gly Pro
145                 150                 155                 160
Ile Cys Leu Pro Glu Leu Arg Glu Gln Phe Glu Ala Gly Phe Ile Cys
                165                 170                 175
Thr Thr Ala Gly Trp Gly Arg Leu Thr Glu Gly Gly Val Leu Ser Gln
            180                 185                 190
Val Leu Gln Glu Val Asn Leu Pro Ile Leu Thr Trp Glu Glu Cys Val
        195                 200                 205
Ala Ala Leu Leu Thr Leu Lys Arg Pro Ile Ser Gly Lys Thr Phe Leu
    210                 215                 220
Cys Thr Gly Phe Pro Asp Gly Gly Arg Asp Ala Cys Gln Gly Asp Ser
225                 230                 235                 240
Gly Gly Ser Leu Met Cys Arg Asn Lys Lys Gly Ala Trp Thr Leu Ala
                245                 250                 255
Gly Val Thr Ser Trp Gly Leu Gly Cys Gly Arg Gly Trp Arg Asn Asn
            260                 265                 270
Val Arg Lys Ser Asp Gln Gly Ser Pro Gly Ile Phe Thr Asp Ile Ser
        275                 280                 285
Lys Val Leu Pro Trp Ile His Glu His Ile Gln Thr Gly Asn Arg Arg
    290                 295                 300
Lys Ser Ser Arg Ala Trp Cys Ser Glu Gln Asp Val Ile Val Ser Gly
305                 310                 315                 320
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Ala Glu Gly Lys Leu His Phe Pro Glu Ser Leu His Leu Tyr Tyr Glu
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Ser Lys Gln Arg Cys Val Trp Thr Leu Leu Val Pro Glu Glu Met His
            340                 345                 350
Val Leu Leu Ser Phe Ser His Leu Asp Val Glu Ser Cys His His Ser
        355                 360                 365
Tyr Leu Ser Met Tyr Ser Leu Glu Asp Arg Pro Ile Gly Lys Phe Cys
    370                 375                 380
Gly Glu Ser Leu Pro Ser Ser Ile Leu Ile Gly Ser Asn Ser Leu Arg
385                 390                 395                 400
Leu Lys Phe Val Ser Asp Ala Thr Asp Tyr Ala Ala Gly Phe Asn Leu
                405                 410                 415
Thr Tyr Lys Ala Leu Lys Pro Asn Tyr Ile Pro Asp Ser Gly Cys Ser
            420                 425                 430
Tyr Leu Thr Val Leu Phe Glu Glu Gly Leu Ile Gln Ser Leu Asn Tyr
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Pro Glu Asn Tyr Ser Asp Lys Ala Asn Cys Asp Trp Ile Phe Gln Ala
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Ser Lys His His Leu Ile Lys Leu Ser Phe Gln Ser Leu Glu Ile Glu
465                 470                 475                 480
Glu Ser Gly Asp Cys Thr Ser Asp Tyr Val Thr Val His Ser Asp Val
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Glu Arg Lys Lys Glu Ile Ala Arg Leu Cys Gly Tyr Asp Val Pro Thr
            500                 505                 510
Pro Val Leu Ser Pro Ser Ser Ile Met Leu Ile Ser Phe Gln Ser Asp
        515                 520                 525
Glu Asn Gly Thr Cys Arg Gly Phe Gln Ala Thr Val Ser Phe Ile Pro
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Lys Ala Gly Lys Lys Ile Glu Leu Pro Thr Leu Trp Phe Pro Val Leu
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Ile Leu Val Met
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<210> 294
<211> 3420
<212> DNA
<213> Homo sapiens

<400> 294

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caagaagtga atggaagcca gagaggaaag ggtattttag acatggaaaa gcaagttgga 1020
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<210> 295
<211> 1134
<212> PRT
<213> Homo sapiens

<400> 295

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His	Pro	Arg	Ser	Leu	Gly	Leu	Lys	Cys	Gly	Ile	Arg	Met	Val	Asn	Met
			20					25				30			
Lys	Ser	Lys	Glu	Pro	Ala	Val	Gly	Ser	Arg	Phe	Phe	Ser	Arg	Ile	Ser
		35					40					45			
Ser	Trp	Arg	Asn	Ser	Thr	Val	Thr	Gly	His	Pro	Trp	Gln	Val	Ser	Leu
	50					55					60				
Lys	Ser	Asp	Glu	His	His	Phe	Cys	Gly	Gly	Ser	Leu	Ile	Gln	Glu	Asp
65					70					75					80
Arg	Val	Val	Thr	Ala	Ala	His	Cys	Leu	Asp	Ser	Leu	Ser	Glu	Lys	Gln

```
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Leu Lys Asn Ile Thr Val Thr Ser Gly Glu Tyr Ser Leu Phe Gln Lys
            100                 105                 110
Asp Lys Gln Glu Gln Asn Ile Pro Val Ser Lys Ile Ile Thr His Pro
        115                 120                 125
Glu Tyr Asn Ser Arg Glu Tyr Met Ser Pro Asp Ile Ala Leu Leu Tyr
    130                 135                 140
Leu Lys His Lys Val Lys Phe Gly Asn Ala Val Gln Pro Ile Cys Leu
145                 150                 155                 160
Pro Asp Ser Asp Asp Lys Val Glu Pro Gly Ile Leu Cys Leu Ser Ser
                165                 170                 175
Gly Trp Gly Lys Ile Ser Lys Thr Ser Glu Tyr Ser Asn Val Leu Gln
            180                 185                 190
Glu Met Glu Leu Pro Ile Met Asp Asp Arg Ala Cys Asn Thr Val Leu
        195                 200                 205
Lys Ser Met Asn Leu Pro Pro Leu Gly Arg Thr Met Leu Cys Ala Gly
    210                 215                 220
Phe Pro Asp Trp Gly Met Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro
225                 230                 235                 240
Leu Val Cys Arg Arg Gly Gly Gly Ile Trp Ile Leu Ala Gly Ile Thr
                245                 250                 255
Ser Trp Val Ala Gly Cys Ala Gly Gly Ser Val Pro Val Arg Asn Asn
            260                 265                 270
His Val Lys Ala Ser Leu Gly Ile Phe Ser Lys Val Ser Glu Leu Met
        275                 280                 285
Asp Phe Ile Thr Gln Asn Leu Phe Thr Gly Leu Asp Arg Gly Gln Pro
    290                 295                 300
Leu Ser Lys Val Gly Ser Arg Tyr Ile Thr Lys Ala Leu Ser Ser Val
305                 310                 315                 320
Gln Glu Val Asn Gly Ser Gln Arg Gly Lys Gly Ile Leu Asp Met Glu
                325                 330                 335
Lys Gln Val Gly Cys Asp His Asp Tyr Val Ser Leu Arg Ser Ser Ser
            340                 345                 350
Gly Val Leu Phe Asn Gln Arg Ser Leu Met Glu Asp Asp Gly Lys Gln
        355                 360                 365
Asn Lys Arg Val Cys Gly Lys Ile Leu Pro Ser Pro Leu Leu Ala Glu
    370                 375                 380
Thr Ser Glu Ala Met Val Pro Phe Val Ser Asp Thr Glu Asp Ser Gly
385                 390                 395                 400
Ser Gly Phe Glu Leu Thr Val Thr Ala Val Gln Lys Ser Glu Ala Gly
                405                 410                 415
Ser Gly Cys Gly Ser Leu Ala Ile Leu Val Glu Glu Gly Thr Asn His
            420                 425                 430
Ser Ala Lys Tyr Pro Asp Leu Tyr Pro Ser Asn Thr Arg Cys His Trp
        435                 440                 445
Phe Ile Cys Ala Pro Glu Lys His Ile Ile Lys Leu Thr Phe Glu Asp
    450                 455                 460
Phe Ala Val Lys Phe Ser Pro Asn Cys Ile Tyr Asp Ala Val Val Ile
465                 470                 475                 480
Tyr Gly Asp Ser Glu Glu Lys His Lys Leu Ala Lys Leu Cys Gly Met
                485                 490                 495
Leu Thr Ile Thr Ser Ile Phe Ser Ser Ser Asn Met Thr Val Ile Tyr
            500                 505                 510
Phe Lys Ser Asp Gly Lys Asn Arg Leu Gln Gly Phe Lys Ala Arg Phe
        515                 520                 525
Thr Ile Leu Pro Ser Glu Ser Leu Asn Lys Phe Glu Pro Lys Leu Pro
    530                 535                 540
Pro Gln Asn Asn Pro Val Ser Thr Val Lys Ala Ile Leu His Asp Val
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545 550 555 560
Cys Gly Ile Pro Pro Phe Ser Pro Gln Trp Leu Ser Arg Arg Ile Ala
565 570 575
Gly Gly Glu Glu Ala Cys Pro His Cys Trp Pro Trp Gln Val Gly Leu
580 585 590
Arg Phe Leu Gly Asp Tyr Gln Cys Gly Gly Ala Ile Ile Asn Pro Val
595 600 605
Trp Ile Leu Thr Ala Ala His Cys Val Gln Leu Lys Asn Asn Pro Leu
610 615 620
Ser Trp Thr Ile Ile Ala Gly Asp His Asp Arg Asn Leu Lys Glu Ser
625 630 635 640
Thr Glu Gln Val Arg Arg Ala Lys His Ile Ile Val His Glu Asp Phe
645 650 655
Asn Thr Leu Ser Tyr Asp Ser Asp Ile Ala Leu Ile Gln Leu Ser Ser
660 665 670
Pro Leu Glu Tyr Asn Ser Val Val Arg Pro Val Cys Leu Pro His Ser
675 680 685
Ala Glu Pro Leu Phe Ser Ser Glu Ile Cys Ala Val Thr Gly Trp Gly
690 695 700
Ser Ile Ser Ala Asp Gly Gly Leu Ala Ser Arg Leu Gln Gln Ile Gln
705 710 715 720
Val His Val Leu Glu Arg Glu Val Cys Glu His Thr Tyr Tyr Ser Ala
725 730 735
His Pro Gly Gly Ile Thr Glu Lys Met Ile Cys Ala Gly Phe Ala Ala
740 745 750
Ser Gly Glu Lys Asp Phe Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
755 760 765
Cys Arg His Glu Asn Gly Pro Phe Val Leu Tyr Gly Ile Val Ser Trp
770 775 780
Gly Ala Gly Cys Val Gln Pro Trp Lys Pro Gly Val Phe Ala Arg Val
785 790 795 800
Met Ile Phe Leu Asp Trp Ile Gln Ser Lys Ile Asn Gly Pro Ala Ser
805 810 815
Leu Gln Thr Asn Asn Lys Cys Lys Thr Leu Lys Gln Gln Leu Pro Pro
820 825 830
Pro Thr Pro Ser Pro Asp Ser Ala Ser Trp Pro Gly Cys Cys Ser Glu
835 840 845
Ala Glu Leu Glu Lys Pro Arg Gly Phe Phe Pro Thr Pro Arg Tyr Leu
850 855 860
Leu Asp Tyr Arg Gly Arg Leu Glu Cys Ser Trp Val Leu Arg Val Ser
865 870 875 880
Ala Ser Ser Met Ala Lys Phe Thr Ile Glu Tyr Leu Ser Leu Leu Gly
885 890 895
Ser Pro Val Cys Gln Asp Ser Val Leu Ile Ile Tyr Glu Glu Arg His
900 905 910
Ser Lys Arg Lys Thr Ala Gly Gly Leu His Gly Arg Arg Leu Tyr Ser
915 920 925
Met Thr Phe Met Ser Pro Gly Pro Leu Val Arg Val Thr Phe His Ala
930 935 940
Leu Val Arg Gly Ala Phe Gly Ile Ser Tyr Ile Asp Leu Lys Val Leu
945 950 955 960
Gly Pro Lys Asp Ser Lys Ile Thr Arg Leu Ser Gln Ser Ser Asn Arg
965 970 975
Glu His Leu Val Pro Cys Glu Asp Val Leu Leu Thr Lys Pro Glu Gly
980 985 990
Ile Met Gln Ile Pro Arg Asn Ser His Arg Thr Thr Met Gly Cys Gln
995 1000 1005
Trp Arg Leu Val Ala Pro Leu Asn His Ile Ile Gln Leu Asn Ile Ile

```
    1010                1015                1020
Asn Phe Pro Met Lys Pro Thr Thr Phe Val Cys His Gly His Leu Arg
1025                1030                1035                1040
Val Tyr Glu Gly Phe Gly Pro Gly Lys Lys Leu Ile Ala Ser Phe Ala
                1045                1050                1055
Gly Thr Leu Ala Met Ile Leu Thr Lys Asp Ile Leu Lys Arg Glu Lys
            1060                1065                1070
Leu Asn Phe Ile Asn Thr Tyr Ile Met His Ile Trp Glu Asn Ser Val
        1075                1080                1085
Tyr Asp Asn Val Arg Ser Val Gly Lys Arg Lys Gln Lys Lys Phe Ala
    1090                1095                1100
Ser Asn Leu Ser Tyr Ser Met Glu Ala Glu Lys Ser Arg Ile Gln Val
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Pro Ala Asp Leu Val Pro Ala Lys Gly Ser Leu Ser Gly Ser
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<210> 296
<211> 2810
<212> DNA
<213> Homo sapiens

<400> 296

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cccaccgaga ttgcagcggc tctggctaat tgggcctctg tgcccgggct attttgaacc 2760
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<210> 297
<211> 766
<212> PRT
<213> Homo sapiens

<400> 297

Met	Thr	Asn	Gly	Thr	Leu	Glu	Pro	Ala	Ala	Glu	Trp	Ser	Val	Leu	Leu
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Gly	Val	His	Ser	Gln	Asp	Gly	Pro	Leu	Asp	Gly	Ala	His	Thr	Arg	Ala
			20					25					30		
Val	Ala	Ala	Ile	Val	Val	Pro	Ala	Asn	Tyr	Ser	Gln	Val	Glu	Leu	Gly
		35					40					45			
Ala	Asp	Leu	Ala	Leu	Leu	Arg	Leu	Ala	Ser	Pro	Ala	Ser	Leu	Gly	Pro
	50					55					60				
Ala	Val	Trp	Pro	Val	Cys	Leu	Pro	Arg	Ala	Ser	His	Arg	Phe	Val	His
65					70					75					80
Gly	Thr	Ala	Cys	Trp	Ala	Thr	Gly	Trp	Gly	Asp	Val	Gln	Glu	Ala	Asp
				85					90					95	
Pro	Leu	Pro	Leu	Pro	Trp	Val	Leu	Gln	Glu	Val	Glu	Leu	Arg	Leu	Leu
			100					105					110		
Gly	Glu	Ala	Thr	Cys	Gln	Cys	Leu	Tyr	Ser	Gln	Pro	Gly	Pro	Phe	Asn
		115					120					125			
Leu	Thr	Leu	Gln	Ile	Leu	Pro	Gly	Met	Leu	Cys	Ala	Gly	Tyr	Pro	Glu
	130					135					140				
Gly	Arg	Arg	Asp	Thr	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys
145					150					155					160
Glu	Glu	Gly	Gly	Arg	Trp	Phe	Gln	Ala	Gly	Ile	Thr	Ser	Phe	Gly	Phe
				165					170					175	
Gly	Cys	Gly	Arg	Arg	Asn	Arg	Pro	Gly	Val	Phe	Thr	Ala	Val	Ala	Thr
			180					185					190		
Tyr	Glu	Ala	Trp	Ile	Arg	Glu	Gln	Val	Met	Gly	Ser	Glu	Pro	Gly	Pro
		195					200					205			
Ala	Phe	Pro	Thr	Gln	Pro	Gln	Lys	Thr	Gln	Ser	Asp	Pro	Gln	Glu	Pro
	210					215					220				
Arg	Glu	Glu	Asn	Cys	Thr	Ile	Ala	Leu	Pro	Glu	Cys	Gly	Lys	Ala	Pro
225					230					235					240
Arg	Pro	Gly	Ala	Trp	Pro	Trp	Glu	Ala	Gln	Val	Met	Val	Pro	Gly	Ser
				245					250					255	
Arg	Pro	Cys	His	Gly	Ala	Leu	Val	Ser	Glu	Ser	Trp	Val	Leu	Ala	Pro
			260					265					270		
Ala	Ser	Cys	Phe	Leu	Asp	Pro	Asn	Ser	Ser	Asp	Ser	Pro	Pro	Arg	Asp
		275					280					285			
Leu	Asp	Ala	Trp	Arg	Val	Leu	Leu	Pro	Ser	Arg	Pro	Arg	Ala	Glu	Arg
	290					295					300				
Val	Ala	Arg	Leu	Val	Gln	His	Glu	Asn	Ala	Ser	Trp	Asp	Asn	Ala	Ser

305 310 315 320
Asp Leu Ala Leu Leu Gln Leu Arg Thr Pro Val Asn Leu Ser Ala Ala
325 330 335
Ser Arg Pro Val Cys Leu Pro His Pro Glu His Tyr Phe Leu Pro Gly
340 345 350
Ser Arg Cys Arg Leu Ala Arg Trp Gly Arg Gly Glu Pro Ala Leu Gly
355 360 365
Pro Gly Ala Leu Leu Glu Ala Glu Leu Leu Gly Gly Trp Trp Cys His
370 375 380
Cys Leu Tyr Gly Arg Gln Gly Ala Ala Val Pro Leu Pro Gly Asp Pro
385 390 395 400
Pro His Ala Leu Cys Pro Ala Tyr Gln Glu Lys Glu Glu Val Gly Ser
405 410 415
Cys Trp Asn Asp Ser Arg Trp Ser Leu Leu Cys Gln Glu Glu Gly Thr
420 425 430
Trp Phe Leu Ala Gly Ile Arg Asp Phe Pro Ser Gly Cys Leu Arg Pro
435 440 445
Arg Ala Phe Phe Pro Leu Gln Thr His Gly Pro Trp Ile Ser His Val
450 455 460
Thr Arg Gly Ala Tyr Leu Glu Asp Gln Leu Ala Trp Asp Trp Gly Pro
465 470 475 480
Asp Gly Glu Glu Thr Glu Thr Gln Thr Cys Pro Pro His Thr Glu His
485 490 495
Gly Ala Cys Gly Leu Arg Leu Glu Ala Ala Pro Val Gly Val Leu Trp
500 505 510
Pro Trp Leu Ala Glu Val His Val Ala Gly Asp Arg Val Cys Thr Gly
515 520 525
Ile Leu Leu Ala Pro Gly Trp Val Leu Ala Ala Thr His Cys Val Leu
530 535 540
Arg Pro Gly Ser Thr Thr Val Pro Tyr Ile Glu Val Tyr Leu Gly Arg
545 550 555 560
Ala Gly Ala Ser Ser Leu Pro Gln Gly His Gln Val Ser Arg Leu Val
565 570 575
Ile Ser Ile Arg Leu Pro Gln His Leu Gly Leu Arg Pro Pro Leu Ala
580 585 590
Leu Leu Glu Leu Ser Ser Arg Val Glu Pro Ser Pro Ser Ala Leu Pro
595 600 605
Ile Cys Leu His Pro Ala Gly Ile Pro Pro Gly Ala Ser Cys Trp Val
610 615 620
Leu Gly Trp Lys Glu Pro Gln Asp Arg Val Pro Val Ala Ala Ala Val
625 630 635 640
Ser Ile Leu Thr Gln Arg Ile Cys Asp Cys Leu Tyr Gln Gly Ile Leu
645 650 655
Pro Pro Gly Thr Leu Cys Val Leu Tyr Ala Glu Gly Gln Glu Asn Arg
660 665 670
Cys Glu Met Thr Ser Ala Pro Pro Leu Leu Cys Gln Met Thr Glu Gly
675 680 685
Ser Trp Ile Leu Val Gly Met Ala Val Gln Gly Ser Arg Glu Leu Phe
690 695 700
Ala Ala Ile Gly Pro Glu Glu Ala Trp Ile Ser Gln Thr Val Gly Glu
705 710 715 720
Ala Asn Leu Leu Pro Pro Ser Gly Ser Pro His Trp Pro Thr Gly Gly
725 730 735
Ser Asn Leu Cys Pro Pro Glu Leu Ala Lys Ala Ser Gly Ser Pro His
740 745 750
Ala Val Tyr Phe Leu Leu Leu Leu Thr Leu Leu Ile Gln Ser
755 760 765

<210> 298
<211> 245
<212> PRT
<213> Homo sapiens

<400> 298
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20 25 30
Lys Gly Glu Ala Gly Arg Pro Gly Arg Arg Gly Arg Pro Gly Leu Lys
35 40 45
Gly Glu Gln Gly Glu Pro Gly Ala Pro Gly Ile Arg Thr Gly Ile Gln
50 55 60
Gly Leu Lys Gly Asp Gln Gly Glu Pro Gly Pro Ser Gly Asn Pro Gly
65 70 75 80
Lys Val Gly Tyr Pro Gly Pro Ser Gly Pro Leu Gly Ala Arg Gly Ile
85 90 95
Pro Gly Ile Lys Gly Thr Lys Gly Ser Pro Gly Asn Ile Lys Asp Gln
100 105 110
Pro Arg Pro Ala Phe Ser Ala Ile Arg Arg Asn Pro Pro Met Gly Gly
115 120 125
Asn Val Val Ile Phe Asp Thr Val Ile Thr Asn Gln Glu Glu Pro Tyr
130 135 140
Gln Asn His Ser Gly Arg Phe Val Cys Thr Val Pro Gly Tyr Tyr Tyr
145 150 155 160
Phe Thr Phe Gln Val Leu Ser Gln Trp Glu Ile Cys Leu Ser Ile Val
165 170 175
Ser Ser Ser Arg Gly Gln Val Arg Arg Ser Leu Gly Phe Cys Asp Thr
180 185 190
Thr Asn Lys Gly Leu Phe Gln Val Val Ser Gly Gly Met Val Leu Gln
195 200 205
Leu Gln Gln Gly Asp Gln Val Trp Val Glu Lys Asp Pro Lys Lys Gly
210 215 220
His Ile Tyr Gln Gly Ser Glu Ala Asp Ser Val Phe Ser Gly Phe Leu
225 230 235 240
Ile Phe Pro Ser Ala
245

<210> 299
<211> 251
<212> PRT
<213> Homo sapiens

<400> 299
Met Lys Ile Pro Trp Gly Ser Ile Pro Val Leu Met Leu Leu Leu Leu
1 5 10 15
Leu Gly Leu Ile Asp Ile Ser Gln Ala Gln Leu Ser Cys Thr Gly Pro
20 25 30
Pro Ala Ile Pro Gly Ile Pro Gly Ile Pro Gly Thr Pro Gly Pro Asp
35 40 45
Gly Gln Pro Gly Thr Pro Gly Ile Lys Gly Glu Lys Gly Leu Pro Gly
50 55 60
Leu Ala Gly Asp His Gly Glu Phe Gly Glu Lys Gly Asp Pro Gly Ile
65 70 75 80
Pro Gly Asn Pro Gly Lys Val Gly Pro Lys Gly Pro Met Gly Pro Lys

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                85                  90                  95
Gly Gly Pro Gly Ala Pro Gly Ala Pro Gly Pro Lys Gly Glu Ser Gly
            100                 105                 110
Asp Tyr Lys Ala Thr Gln Lys Ile Ala Phe Ser Ala Thr Arg Thr Ile
        115                 120                 125
Asn Val Pro Leu Arg Arg Asp Gln Thr Ile Arg Phe Asp His Val Ile
    130                 135                 140
Thr Asn Met Asn Asn Asn Tyr Glu Pro Arg Ser Gly Lys Phe Thr Cys
145                 150                 155                 160
Lys Val Pro Gly Leu Tyr Tyr Phe Thr Tyr His Ala Ser Ser Arg Gly
                165                 170                 175
Asn Leu Cys Val Asn Leu Met Arg Gly Arg Glu Arg Ala Gln Lys Val
            180                 185                 190
Val Thr Phe Cys Asp Tyr Ala Tyr Asn Thr Phe Gln Val Thr Thr Gly
        195                 200                 205
Gly Met Val Leu Lys Leu Glu Gln Gly Glu Asn Val Phe Leu Gln Ala
    210                 215                 220
Thr Asp Lys Asn Ser Leu Leu Gly Met Glu Gly Ala Asn Ser Ile Phe
225                 230                 235                 240
Ser Gly Phe Leu Leu Phe Pro Asp Met Glu Ala
                245                 250
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<210> 300
<211> 245
<212> PRT
<213> Homo sapiens

<400> 300

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Met Asp Val Gly Pro Ser Ser Leu Pro His Leu Gly Leu Lys Leu Leu
 1                5                  10                  15
Leu Leu Leu Leu Leu Leu Pro Leu Arg Gly Gln Ala Asn Thr Gly Cys
            20                  25                  30
Tyr Gly Ile Pro Gly Met Pro Gly Leu Pro Gly Ala Pro Gly Lys Asp
        35                  40                  45
Gly Tyr Asp Gly Leu Pro Gly Pro Lys Gly Glu Pro Gly Ile Pro Ala
    50                  55                  60
Ile Pro Gly Ile Arg Gly Pro Lys Gly Gln Lys Gly Glu Pro Gly Leu
65                  70                  75                  80
Pro Gly His Pro Gly Lys Asn Gly Pro Met Gly Pro Pro Gly Met Pro
                85                  90                  95
Gly Val Pro Gly Pro Met Gly Ile Pro Gly Glu Pro Gly Glu Glu Gly
            100                 105                 110
Arg Tyr Lys Gln Lys Phe Gln Ser Val Phe Thr Val Thr Arg Gln Thr
        115                 120                 125
His Gln Pro Pro Ala Pro Asn Ser Leu Ile Arg Phe Asn Ala Val Leu
    130                 135                 140
Thr Asn Pro Gln Gly Asp Tyr Asp Thr Ser Thr Gly Lys Phe Thr Cys
145                 150                 155                 160
Lys Val Pro Gly Leu Tyr Tyr Phe Val Tyr His Ala Ser His Thr Ala
                165                 170                 175
Asn Leu Cys Val Leu Leu Tyr Arg Ser Gly Val Lys Val Val Thr Phe
            180                 185                 190
Cys Gly His Thr Ser Lys Thr Asn Gln Val Asn Ser Gly Gly Val Leu
        195                 200                 205
Leu Arg Leu Gln Val Gly Glu Glu Val Trp Leu Ala Val Asn Asp Tyr
    210                 215                 220
Tyr Asp Met Val Gly Ile Gln Gly Ser Asp Ser Val Phe Ser Gly Phe
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225 230 235 240
Leu Leu Phe Pro Asp
245

<210> 301
<211> 2526
<212> DNA
<213> Homo sapiens

<400> 301
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tgtggctctt gtacctcctg gtgccggccc tgttctgcag ggcaggaggc tccattccca 120
tccctcagaa gttatttggg gaggtgactt cccctctgtt ccccaagcct taccccaaca 180
actttgaaac aaccactgtg atcacagtcc ccacgggata cagggtgaag ctcgtcttcc 240
agcagtttga cctggagcct tctgaaggct gcttctatga ttatgtcaag atctctgctg 300
ataagaaaag cctggggagg ttctgtgggc aactgggttc tccactgggc aacccccccgg 360
gaaagaagga atttatgtcc caagggaaca agatgctgct gaccttccac acagacttct 420
ccaacgagga gaatgggacc atcatgttct acaagggctt cctggcctac taccaagctg 480
tggaccttga tgaatgtgct tcccggagca aattagggga ggaggatccc cagccccagt 540
gccagcacct gtgtcacaac tacgttggag gctacttctg ttcctgccgt ccaggctatg 600
agcttcagga agacaggcat tcctgccagg ctgagtgcag cagcgagctg tacacggagg 660
catcaggcta catctccagc ctggagtacc ctcggtccta ccccctgac ctgcgctgca 720
actacagcat ccgggtggag cggggcctca ccctgcacct caagttcctg gagccttttg 780
atattgatga ccaccagcaa gtacactgcc cctatgacca gctacagatc tatgccaacg 840
ggaagaacat tggcgagttc tgtgggaagc aaaggccccc cgacctcgac accagcagca 900
atgctgtgga tctgctgttc ttcacagatg agtcgggggga cagccggggc tggaagctgc 960
gctacaccac cgagatcatc aagtgccccc agcccaagac cctagacgag ttcaccatca 1020
tccagaacct gcagcctcag taccagttcc gtgactactt cattgctacc tgcaagcaag 1080
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acctgcctaa tggtgacttc cgttacacca ccacaatggg agtgaacacc tacaaggccc 1260
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gagagaagat tcctcggtgc ttgccagtgt gtgggaagcc cgtgaacccc gtggaacaga 1440
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tgggccacac aaatgtggaa gagctcatga agctaggaaa tcaccccatc cgcagggtca 1680
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acgatacctt ctacgacctg ggcttgatgg gctatgtcag tggcttcggg gtcatggagg 1860
agaagattgc tcatgacctc aggtttgtcc gtctgcccgt agctaatcca caggcctgtg 1920
agaactggct ccggggaaag aataggatgg atgtgttctc tcaaaacatg ttctgtgctg 1980
gacacccatc tctaaagcag gacgcctgcc agggggatag tgggggcgtt tttgcagtaa 2040
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aaaaaa 2526

<210> 302
<211> 705
<212> PRT

<213> Homo sapiens

<400> 302

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Met Trp Leu Leu Tyr Leu Leu Val Pro Ala Leu Phe Cys Arg Ala Gly
 1               5                  10                  15
Gly Ser Ile Pro Ile Pro Gln Lys Leu Phe Gly Glu Val Thr Ser Pro
            20                  25                  30
Leu Phe Pro Lys Pro Tyr Pro Asn Asn Phe Glu Thr Thr Thr Val Ile
        35                  40                  45
Thr Val Pro Thr Gly Tyr Arg Val Lys Leu Val Phe Gln Gln Phe Asp
    50                  55                  60
Leu Glu Pro Ser Glu Gly Cys Phe Tyr Asp Tyr Val Lys Ile Ser Ala
65                  70                  75                  80
Asp Lys Lys Ser Leu Gly Arg Phe Cys Gly Gln Leu Gly Ser Pro Leu
                85                  90                  95
Gly Asn Pro Pro Gly Lys Lys Glu Phe Met Ser Gln Gly Asn Lys Met
            100                 105                 110
Leu Leu Thr Phe His Thr Asp Phe Ser Asn Glu Glu Asn Gly Thr Ile
        115                 120                 125
Met Phe Tyr Lys Gly Phe Leu Ala Tyr Tyr Gln Ala Val Asp Leu Asp
    130                 135                 140
Glu Cys Ala Ser Arg Ser Lys Ser Gly Glu Glu Asp Pro Gln Pro Gln
145                 150                 155                 160
Cys Gln His Leu Cys His Asn Tyr Val Gly Gly Tyr Phe Cys Ser Cys
                165                 170                 175
Arg Pro Gly Tyr Glu Leu Gln Glu Asp Arg His Ser Cys Gln Ala Glu
            180                 185                 190
Cys Ser Ser Glu Leu Tyr Thr Glu Ala Ser Gly Tyr Ile Ser Ser Leu
        195                 200                 205
Glu Tyr Pro Arg Ser Tyr Pro Pro Asp Leu Arg Cys Asn Tyr Ser Ile
    210                 215                 220
Arg Val Glu Arg Gly Leu Thr Leu His Leu Lys Phe Leu Glu Pro Phe
225                 230                 235                 240
Asp Ile Asp Asp His Gln Gln Val His Cys Pro Tyr Asp Gln Leu Gln
                245                 250                 255
Ile Tyr Ala Asn Gly Lys Asn Ile Gly Glu Phe Cys Gly Lys Gln Arg
            260                 265                 270
Pro Pro Asp Leu Asp Thr Ser Ser Asn Ala Val Asp Leu Leu Phe Phe
        275                 280                 285
Thr Asp Glu Ser Gly Asp Ser Arg Gly Trp Lys Leu Arg Tyr Thr Thr
    290                 295                 300
Glu Ile Ile Lys Cys Pro Gln Pro Lys Thr Leu Asp Glu Phe Thr Ile
305                 310                 315                 320
Ile Gln Asn Leu Gln Pro Gln Tyr Gln Phe Arg Asp Tyr Phe Ile Ala
                325                 330                 335
Thr Cys Lys Gln Gly Tyr Gln Leu Ile Glu Gly Asn Gln Val Leu His
            340                 345                 350
Ser Phe Thr Ala Val Cys Gln Asp Asp Gly Thr Trp His Arg Ala Met
        355                 360                 365
Pro Arg Cys Lys Ile Lys Asp Cys Gly Gln Pro Arg Asn Leu Pro Asn
    370                 375                 380
Gly Asp Phe Arg Tyr Thr Thr Thr Met Gly Val Asn Thr Tyr Lys Ala
385                 390                 395                 400
Arg Ile Gln Tyr Tyr Cys His Glu Pro Tyr Tyr Lys Met Gln Thr Arg
                405                 410                 415
Ala Gly Ser Arg Glu Ser Glu Gln Gly Val Tyr Thr Cys Thr Ala Gln
            420                 425                 430
Gly Ile Trp Lys Asn Glu Gln Lys Gly Glu Lys Ile Pro Arg Cys Leu
```

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        435                 440                 445
Pro Val Cys Gly Lys Pro Val Asn Pro Val Glu Gln Arg Gln Arg Ile
    450                 455                 460
Ile Gly Gly Gln Lys Ala Lys Met Gly Asn Phe Pro Trp Gln Val Phe
465                 470                 475                 480
Thr Asn Ile His Gly Arg Gly Gly Gly Ala Leu Leu Gly Asp Arg Trp
                485                 490                 495
Ile Leu Thr Ala Ala His Thr Leu Tyr Pro Lys Glu His Glu Ala Gln
            500                 505                 510
Ser Asn Ala Ser Leu Asp Val Phe Leu Gly His Thr Asn Val Glu Glu
        515                 520                 525
Leu Met Lys Leu Gly Asn His Pro Ile Arg Arg Val Ser Val His Pro
    530                 535                 540
Asp Tyr Arg Gln Asp Glu Ser Tyr Asn Phe Glu Gly Asp Ile Ala Leu
545                 550                 555                 560
Leu Glu Leu Glu Asn Ser Val Thr Leu Gly Pro Asn Leu Leu Pro Ile
                565                 570                 575
Cys Leu Pro Asp Asn Asp Thr Phe Tyr Asp Leu Gly Leu Met Gly Tyr
            580                 585                 590
Val Ser Gly Phe Gly Val Met Glu Glu Lys Ile Ala His Asp Leu Arg
        595                 600                 605
Phe Val Arg Leu Pro Val Ala Asn Pro Gln Ala Cys Glu Asn Trp Leu
    610                 615                 620
Arg Gly Lys Asn Arg Met Asp Val Phe Ser Gln Asn Met Phe Cys Ala
625                 630                 635                 640
Gly His Pro Ser Leu Lys Gln Asp Ala Cys Gln Gly Asp Ser Gly Gly
                645                 650                 655
Val Phe Ala Val Arg Asp Pro Asn Thr Asp Arg Trp Val Ala Thr Gly
            660                 665                 670
Ile Val Ser Trp Gly Ile Gly Cys Ser Arg Gly Tyr Gly Phe Tyr Thr
        675                 680                 685
Lys Val Leu Asn Tyr Val Asp Trp Ile Lys Lys Glu Met Glu Glu Glu
    690                 695                 700
Asp
705
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<210> 303
<211> 2714
<212> DNA
<213> Homo sapiens

<400> 303
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aaggccctgt gctgctgtcc ctgggggcca gaggggttgc ccagcatgcc cactggcagg 120
agagagggaa ctgacccact tgctcctacc agcttctgaa ggctccaaag tccggaggtg 180
cagaaagcca ggaccaagag acaggcagct caccagggtg gacaaatcgc cagagatgtg 240
gtgcattgtc ctgttttcac ttttggcatg ggtttatgct gagcctacca tgtatgggga 300
gatcctgtcc cctaactatc ctcaggcata tcccagtgag gtagagaaat cttgggacat 360
agaagttcct gaagggtatg ggattcacct ctacttcacc catctggaca ttgagctgtc 420
agagaactgt gcgtatgact cagtgcagat aatctcagga gacactgaag aagggaggct 480
ctgtggacag aggagcagta acaatcccca ctctccaatt gtggaagagt tccaagtccc 540
atacaacaaa ctccaggtga tctttaagtc agacttttcc aatgaagagc gttttacggg 600
gtttgctgca tactatgttg ccacagacat aaatgaatgc acagattttg tagatgtccc 660
ttgtagccac ttctgcaaca atttcattgg tggttacttc tgctcctgcc ccccggaata 720
tttcctccat gatgacatga agaattgcgg agttaattgc agtggggatg tattcactgc 780
actgattggg gagattgcaa gtcccaatta tcccaaacca tatccagaga actcaaggtg 840
tgaataccag atccggttgg agaaagggtt ccaagtggtg gtgaccttgc ggagagaaga 900

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gccaacaatg tatgttgggt ccacctcagt gcagacctca cggctggcaa aatccaagat 1740
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<210> 304
<211> 688
<212> PRT
<213> Homo sapiens

<400> 304
Met Trp Cys Ile Val Leu Phe Ser Leu Leu Ala Trp Val Tyr Ala Glu
1 5 10 15
Pro Thr Met Tyr Gly Glu Ile Leu Ser Pro Asn Tyr Pro Gln Ala Tyr
20 25 30
Pro Ser Glu Val Glu Lys Ser Trp Asp Ile Glu Val Pro Glu Gly Tyr
35 40 45
Gly Ile His Leu Tyr Phe Thr His Leu Asp Ile Glu Leu Ser Glu Asn
50 55 60
Cys Ala Tyr Asp Ser Val Gln Ile Ile Ser Gly Asp Thr Glu Glu Gly
65 70 75 80
Arg Leu Cys Gly Gln Arg Ser Ser Asn Asn Pro His Ser Pro Ile Val
85 90 95
Glu Glu Phe Gln Val Pro Tyr Asn Lys Leu Gln Val Ile Phe Lys Ser
100 105 110
Asp Phe Ser Asn Glu Glu Arg Phe Thr Gly Phe Ala Ala Tyr Tyr Val
115 120 125
Ala Thr Asp Ile Asn Glu Cys Thr Asp Phe Val Asp Val Pro Cys Ser
130 135 140
His Phe Cys Asn Asn Phe Ile Gly Gly Tyr Phe Cys Ser Cys Pro Pro
145 150 155 160

Glu Tyr Phe Leu His Asp Asp Met Lys Asn Cys Gly Val Asn Cys Ser
165 170 175
Gly Asp Val Phe Thr Ala Leu Ile Gly Glu Ile Ala Ser Pro Asn Tyr
180 185 190
Pro Lys Pro Tyr Pro Glu Asn Ser Arg Cys Glu Tyr Gln Ile Arg Leu
195 200 205
Glu Lys Gly Phe Gln Val Val Val Thr Leu Arg Arg Glu Asp Phe Asp
210 215 220
Val Glu Ala Ala Asp Ser Ala Gly Asn Cys Leu Asp Ser Leu Val Phe
225 230 235 240
Val Ala Gly Asp Arg Gln Phe Gly Pro Tyr Cys Gly His Gly Phe Pro
245 250 255
Gly Pro Leu Asn Ile Glu Thr Lys Ser Asn Ala Leu Asp Ile Ile Phe
260 265 270
Gln Thr Asp Leu Thr Gly Gln Lys Lys Gly Trp Lys Leu Arg Tyr His
275 280 285
Gly Asp Pro Met Pro Cys Pro Lys Glu Asp Thr Pro Asn Ser Val Trp
290 295 300
Glu Pro Ala Lys Ala Lys Tyr Val Phe Arg Asp Val Val Gln Ile Thr
305 310 315 320
Cys Leu Asp Gly Phe Glu Val Val Glu Gly Arg Val Gly Ala Thr Ser
325 330 335
Phe Tyr Ser Thr Cys Gln Ser Asn Gly Lys Trp Ser Asn Ser Lys Leu
340 345 350
Lys Cys Gln Pro Val Asp Cys Gly Ile Pro Glu Ser Ile Glu Asn Gly
355 360 365
Lys Val Glu Asp Pro Glu Ser Thr Leu Phe Gly Ser Val Ile Arg Tyr
370 375 380
Thr Cys Glu Glu Pro Tyr Tyr Tyr Met Glu Asn Gly Gly Gly Gly Glu
385 390 395 400
Tyr His Cys Ala Gly Asn Gly Ser Trp Val Asn Glu Val Leu Gly Pro
405 410 415
Glu Leu Pro Lys Cys Val Pro Val Cys Gly Val Pro Arg Glu Pro Phe
420 425 430
Glu Glu Lys Gln Arg Ile Ile Gly Gly Ser Asp Ala Asp Ile Lys Asn
435 440 445
Phe Pro Trp Gln Val Phe Phe Asp Asn Pro Trp Ala Gly Gly Ala Leu
450 455 460
Ile Asn Glu Tyr Trp Val Leu Thr Ala Ala His Val Val Glu Gly Asn
465 470 475 480
Arg Glu Pro Thr Met Tyr Val Gly Ser Thr Ser Val Gln Thr Ser Arg
485 490 495
Leu Ala Lys Ser Lys Met Leu Thr Pro Glu His Val Phe Ile His Pro
500 505 510
Gly Trp Lys Leu Leu Glu Val Pro Glu Gly Arg Thr Asn Phe Asp Asn
515 520 525
Asp Ile Ala Leu Val Arg Leu Lys Asp Pro Val Lys Met Gly Pro Thr
530 535 540
Val Ser Pro Ile Cys Leu Pro Gly Thr Ser Ser Asp Tyr Asn Leu Met
545 550 555 560
Asp Gly Asp Leu Gly Leu Ile Ser Gly Trp Gly Arg Thr Glu Lys Arg
565 570 575
Asp Arg Ala Val Arg Leu Lys Ala Ala Arg Leu Pro Val Ala Pro Leu
580 585 590
Arg Lys Cys Lys Glu Val Lys Val Glu Lys Pro Thr Ala Asp Ala Glu
595 600 605
Ala Tyr Val Phe Thr Pro Asn Met Ile Cys Ala Gly Gly Glu Lys Gly
610 615 620

```
Met Asp Ser Cys Lys Gly Asp Ser Gly Gly Ala Phe Ala Val Gln Asp
625                 630                 635                 640
Pro Asn Asp Lys Thr Lys Phe Tyr Ala Ala Gly Leu Val Ser Trp Gly
                645                 650                 655
Pro Gln Cys Gly Thr Tyr Gly Leu Tyr Thr Arg Val Lys Asn Tyr Val
            660                 665                 670
Asp Trp Ile Met Lys Thr Met Gln Glu Asn Ser Thr Pro Arg Glu Asp
        675                 680                 685
```

<210> 305
<211> 252
<212> PRT
<213> Homo sapiens

<400> 305

```
Met Phe Phe Trp Cys Ala Cys Cys Leu Met Val Ala Trp Arg Val Ser
 1               5                  10                  15
Ala Ser Asp Ala Glu His Cys Pro Glu Leu Pro Pro Val Asp Asn Ser
            20                  25                  30
Ile Phe Val Ala Lys Glu Val Glu Gly Gln Ile Leu Gly Thr Tyr Val
        35                  40                  45
Cys Ile Lys Gly Tyr His Leu Val Gly Lys Lys Thr Leu Phe Cys Asn
    50                  55                  60
Ala Ser Lys Glu Trp Asp Asn Thr Thr Thr Glu Cys Arg Leu Gly His
65                  70                  75                  80
Cys Pro Asp Pro Val Leu Val Asn Gly Glu Phe Ser Ser Ser Gly Pro
                85                  90                  95
Val Asn Val Ser Asp Lys Ile Thr Phe Met Cys Asn Asp His Tyr Ile
            100                 105                 110
Leu Lys Gly Ser Asn Arg Ser Gln Cys Leu Glu Asp His Thr Trp Ala
        115                 120                 125
Pro Pro Phe Pro Ile Cys Lys Ser Arg Asp Cys Asp Pro Pro Gly Asn
    130                 135                 140
Pro Val His Gly Tyr Phe Glu Gly Asn Asn Phe Thr Leu Gly Ser Thr
145                 150                 155                 160
Ile Ser Tyr Tyr Cys Glu Asp Arg Tyr Tyr Leu Val Gly Val Gln Glu
                165                 170                 175
Gln Gln Cys Val Asp Gly Glu Trp Ser Ser Ala Leu Pro Val Cys Lys
            180                 185                 190
Leu Ile Gln Glu Ala Pro Lys Pro Glu Cys Glu Lys Ala Leu Leu Ala
        195                 200                 205
Phe Gln Glu Ser Lys Asn Leu Cys Glu Ala Met Glu Asn Phe Met Gln
    210                 215                 220
Gln Leu Lys Glu Ser Gly Met Thr Met Glu Glu Leu Lys Tyr Ser Leu
225                 230                 235                 240
Glu Leu Lys Lys Ala Glu Leu Lys Ala Lys Leu Leu
                245                 250
```

<210> 306
<211> 597
<212> PRT
<213> Homo sapiens

<400> 306

```
Met His Pro Pro Lys Thr Pro Ser Gly Ala Leu His Arg Lys Arg Lys
 1               5                  10                  15
```

Met Ala Ala Trp Pro Phe Ser Arg Leu Trp Lys Val Ser Asp Pro Ile
20 25 30
Leu Phe Gln Met Thr Leu Ile Ala Ala Leu Leu Pro Ala Val Leu Gly
35 40 45
Asn Cys Gly Pro Pro Pro Thr Leu Ser Phe Ala Ala Pro Met Asp Ile
50 55 60
Thr Leu Thr Glu Thr Arg Phe Lys Thr Gly Thr Thr Leu Lys Tyr Thr
65 70 75 80
Cys Leu Pro Gly Tyr Val Arg Ser His Ser Thr Gln Thr Leu Thr Cys
85 90 95
Asn Ser Asp Gly Glu Trp Val Tyr Asn Thr Phe Cys Ile Tyr Lys Arg
100 105 110
Cys Arg His Pro Gly Glu Leu Arg Asn Gly Gln Val Glu Ile Lys Thr
115 120 125
Asp Leu Ser Phe Gly Ser Gln Ile Glu Phe Ser Cys Ser Glu Gly Phe
130 135 140
Phe Leu Ile Gly Ser Thr Thr Ser Arg Cys Glu Val Gln Asp Arg Gly
145 150 155 160
Val Gly Trp Ser His Pro Leu Pro Gln Cys Glu Ile Val Lys Cys Lys
165 170 175
Pro Pro Pro Asp Ile Arg Asn Gly Arg His Ser Gly Glu Glu Asn Phe
180 185 190
Tyr Ala Tyr Gly Phe Ser Val Thr Tyr Ser Cys Asp Pro Arg Phe Ser
195 200 205
Leu Leu Gly His Ala Ser Ile Ser Cys Thr Val Glu Asn Glu Thr Ile
210 215 220
Gly Val Trp Arg Pro Ser Pro Pro Thr Cys Glu Lys Ile Thr Cys Arg
225 230 235 240
Lys Pro Asp Val Ser His Gly Glu Met Val Ser Gly Phe Gly Pro Ile
245 250 255
Tyr Asn Tyr Lys Asp Thr Ile Val Phe Lys Cys Gln Lys Gly Phe Val
260 265 270
Leu Arg Gly Ser Ser Val Ile His Cys Asp Ala Asp Ser Lys Trp Asn
275 280 285
Pro Ser Pro Pro Ala Cys Glu Pro Asn Ser Cys Ile Asn Leu Pro Asp
290 295 300
Ile Pro His Ala Ser Trp Glu Thr Tyr Pro Arg Pro Thr Lys Glu Asp
305 310 315 320
Val Tyr Val Val Gly Thr Val Leu Arg Tyr Arg Cys His Pro Gly Tyr
325 330 335
Lys Pro Thr Thr Asp Glu Pro Thr Thr Val Ile Cys Gln Lys Asn Leu
340 345 350
Arg Trp Thr Pro Tyr Gln Gly Cys Glu Ala Leu Cys Cys Pro Glu Pro
355 360 365
Lys Leu Asn Asn Gly Glu Ile Thr Gln His Arg Lys Ser Arg Pro Ala
370 375 380
Asn His Cys Val Tyr Phe Tyr Gly Asp Glu Ile Ser Phe Ser Cys His
385 390 395 400
Glu Thr Ser Arg Phe Ser Ala Ile Cys Gln Gly Asp Gly Thr Trp Ser
405 410 415
Pro Arg Thr Pro Ser Cys Gly Asp Ile Cys Asn Phe Pro Pro Lys Ile
420 425 430
Ala His Gly His Tyr Lys Gln Ser Ser Ser Tyr Ser Phe Phe Lys Glu
435 440 445
Glu Ile Ile Tyr Glu Cys Asp Lys Gly Tyr Ile Leu Val Gly Gln Ala
450 455 460
Lys Leu Ser Cys Ser Tyr Ser His Trp Ser Ala Pro Ala Pro Gln Cys
465 470 475 480

```
Lys Ala Leu Cys Arg Lys Pro Glu Leu Val Asn Gly Arg Leu Ser Val
                485                 490                 495
Asp Lys Asp Gln Tyr Val Glu Pro Glu Asn Val Thr Ile Gln Cys Asp
            500                 505                 510
Ser Gly Tyr Gly Val Val Gly Pro Gln Ser Ile Thr Cys Ser Gly Asn
        515                 520                 525
Arg Thr Trp Tyr Pro Glu Val Pro Lys Cys Glu Trp Glu Thr Pro Glu
    530                 535                 540
Gly Cys Glu Gln Val Leu Thr Gly Lys Arg Leu Met Gln Cys Leu Pro
545                 550                 555                 560
Asn Pro Glu Asp Val Lys Met Ala Leu Glu Val Tyr Lys Leu Ser Leu
                565                 570                 575
Glu Ile Glu Gln Leu Glu Leu Gln Arg Asp Ser Ala Arg Gln Ser Thr
            580                 585                 590
Leu Asp Lys Glu Leu
        595
```

<210> 307
<211> 1963
<212> DNA
<213> Homo sapiens

<400> 307

```
cgaacacctc caacatgaag cttcttcatg ttttcctgtt atttctgtgc ttccacttaa 60
ggttttgcaa ggtcacttat acatctcaag aggatctggt ggagaaaaag tgcttagcaa 120
aaaaatatac tcacctctcc tgcgataaag tcttctgcca gccatggcag agatgcattg 180
agggcacctg tgtttgtaaa ctaccgtatc agtgcccaaa gaatggcact gcagtgtgtg 240
caactaacag gagaagcttc ccaacatact gtcaacaaaa gagtttggaa tgtcttcatc 300
cagggacaaa gtttttaaat aacggaacat gcacagccga aggaaagttt agtgtttcct 360
tgaagcatgg aaatacagat tcagagggaa tagttgaagt aaaacttgtg gaccaagata 420
agacaatgtt catatgcaaa agcagctgga gcatgaggga agccaacgtg gcctgccttg 480
accttgggtt tcaacaaggt gctgatactc aaagaaggtt taagttgtct gatctctcta 540
taaattccac tgaatgtcta catgtgcatt gccgaggatt agagaccagt ttggctgaat 600
gtacttttac taagagaaga actatgggtt accaggattt cgctgatgtg gtttgttata 660
cacagaaagc agattctcca atggatgact tctttcagtg tgtgaatggg aaatacattt 720
ctcagatgaa agcctgtgat ggtatcaatg attgtggaga ccaaagtgat gaactgtgtt 780
gtaaagcatg ccaaggcaaa ggcttccatt gcaaatcggg tgtttgcatt ccaagccagt 840
atcaatgcaa tggtgaggtg gactgcatta caggggaaga tgaagttggc tgtgcaggct 900
ttgcatctgt ggctcaagaa gaaacagaaa ttttgactgc tgacatggat gcagaaagaa 960
gacggataaa atcattatta cctaaactat cttgtggagt taaaaacaga atgcacattc 1020
gaaggaaacg aattgtggga ggaaagcgag cacaactggg agacctccca tggcaggtgg 1080
caattaagga tgccagtgga atcacctgtg ggggaattta tattggtggc tgttggattc 1140
tgactgctgc acattgtctc agagccagta aaactcatcg ttaccaaata tggacaacag 1200
tagtagactg gatacacccc gaccttaaac gtatagtaat tgaatacgtg gatagaatta 1260
ttttccatga aaactacaat gcaggcactt accaaaatga catcgctttg attgaaatga 1320
aaaaagacgg aaacaaaaaa gattgtgagc tgcctcgttc catccctgcc tgtgtccgct 1380
ggtctcctta cctattccaa cctaatgata catgcatcgt ttctggctgg ggacgagaaa 1440
aagataacga aagagtcttt tcacttcagt ggggtgaagt taaactaata agcaactgct 1500
ctaagtttta cggaaatcgt ttctatgaaa aagaaatgga atgtgcaggt acatatgatg 1560
gttccatcga tgcctgtaaa ggggactctg gaggcccctt agtctgtatg gatgccaaca 1620
atgtgactta tgtctggggt gttgtgagtt gggggggaaaa ctgtggaaaa ccagagttcc 1680
caggttttta caccaaagtg gccaattatt ttgactggat tagctaccat gtaggaaggc 1740
cttttatttc tcagtacaat gtataaaatt gtgatctctc tcttcattct attcttttttc 1800
tctcaagagt tccatttaat ggaaataaaa cggtataatt aataattctc taggggggaa 1860
aaatgaagca aatctcattg gatattttta aaggtctcca cagagtttat gccatattgg 1920
aattttgttg tataattctc aaataaatat tttggtgaag cat                  1963
```

<210> 308
<211> 583
<212> PRT
<213> Homo sapiens

<400> 308
Met Lys Leu Leu His Val Phe Leu Leu Phe Leu Cys Phe His Leu Arg
1 5 10 15
Phe Cys Lys Val Thr Tyr Thr Ser Gln Glu Asp Leu Val Glu Lys Lys
20 25 30
Cys Leu Ala Lys Lys Tyr Thr His Leu Ser Cys Asp Lys Val Phe Cys
35 40 45
Gln Pro Trp Gln Arg Cys Ile Glu Gly Thr Cys Val Cys Lys Leu Pro
50 55 60
Tyr Gln Cys Pro Lys Asn Gly Thr Ala Val Cys Ala Thr Asn Arg Arg
65 70 75 80
Ser Phe Pro Thr Tyr Cys Gln Gln Lys Ser Leu Glu Cys Leu His Pro
85 90 95
Gly Thr Lys Phe Leu Asn Asn Gly Thr Cys Thr Ala Glu Gly Lys Phe
100 105 110
Ser Val Ser Leu Lys His Gly Asn Thr Asp Ser Glu Gly Ile Val Glu
115 120 125
Val Lys Leu Val Asp Gln Asp Lys Thr Met Phe Ile Cys Lys Ser Ser
130 135 140
Trp Ser Met Arg Glu Ala Asn Val Ala Cys Leu Asp Leu Gly Phe Gln
145 150 155 160
Gln Gly Ala Asp Thr Gln Arg Arg Phe Lys Leu Ser Asp Leu Ser Ile
165 170 175
Asn Ser Thr Glu Cys Leu His Val His Cys Arg Gly Leu Glu Thr Ser
180 185 190
Leu Ala Glu Cys Thr Phe Thr Lys Arg Arg Thr Met Gly Tyr Gln Asp
195 200 205
Phe Ala Asp Val Val Cys Tyr Thr Gln Lys Ala Asp Ser Pro Met Asp
210 215 220
Asp Phe Phe Gln Cys Val Asn Gly Lys Tyr Ile Ser Gln Met Lys Ala
225 230 235 240
Cys Asp Gly Ile Asn Asp Cys Gly Asp Gln Ser Asp Glu Leu Cys Cys
245 250 255
Lys Ala Cys Gln Gly Lys Gly Phe His Cys Lys Ser Gly Val Cys Ile
260 265 270
Pro Ser Gln Tyr Gln Cys Asn Gly Glu Val Asp Cys Ile Thr Gly Glu
275 280 285
Asp Glu Val Gly Cys Ala Gly Phe Ala Ser Val Ala Gln Glu Glu Thr
290 295 300
Glu Ile Leu Thr Ala Asp Met Asp Ala Glu Arg Arg Arg Ile Lys Ser
305 310 315 320
Leu Leu Pro Lys Leu Ser Cys Gly Val Lys Asn Arg Met His Ile Arg
325 330 335
Arg Lys Arg Ile Val Gly Gly Lys Arg Ala Gln Leu Gly Asp Leu Pro
340 345 350
Trp Gln Val Ala Ile Lys Asp Ala Ser Gly Ile Thr Cys Gly Gly Ile
355 360 365
Tyr Ile Gly Gly Cys Trp Ile Leu Thr Ala Ala His Cys Leu Arg Ala
370 375 380
Ser Lys Thr His Arg Tyr Gln Ile Trp Thr Thr Val Val Asp Trp Ile
385 390 395 400
His Pro Asp Leu Lys Arg Ile Val Ile Glu Tyr Val Asp Arg Ile Ile
405 410 415

```
Phe His Glu Asn Tyr Asn Ala Gly Thr Tyr Gln Asn Asp Ile Ala Leu
            420                 425                 430
Ile Glu Met Lys Lys Asp Gly Asn Lys Lys Asp Cys Glu Leu Pro Arg
        435                 440                 445
Ser Ile Pro Ala Cys Val Pro Trp Ser Pro Tyr Leu Phe Gln Pro Asn
    450                 455                 460
Asp Thr Cys Ile Val Ser Gly Trp Gly Arg Glu Lys Asp Asn Glu Arg
465                 470                 475                 480
Val Phe Ser Leu Gln Trp Gly Glu Val Lys Leu Ile Ser Asn Cys Ser
                485                 490                 495
Lys Phe Tyr Gly Asn Arg Phe Tyr Glu Lys Glu Met Glu Cys Ala Gly
            500                 505                 510
Thr Tyr Asp Gly Ser Ile Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro
        515                 520                 525
Leu Val Cys Met Asp Ala Asn Asn Val Thr Tyr Val Trp Gly Val Val
    530                 535                 540
Ser Trp Gly Glu Asn Cys Gly Lys Pro Glu Phe Pro Gly Val Tyr Thr
545                 550                 555                 560
Lys Val Ala Asn Tyr Phe Asp Trp Ile Ser Tyr His Val Gly Arg Pro
                565                 570                 575
Phe Ile Ser Gln Tyr Asn Val
            580
```

<210> 309
<211> 449
<212> PRT
<213> Homo sapiens

<400> 309

```
Met Met Lys Thr Leu Leu Leu Phe Val Gly Leu Leu Leu Thr Trp Glu
 1               5                  10                  15
Ser Gly Gln Val Leu Gly Asp Gln Thr Val Ser Asp Asn Glu Leu Gln
            20                  25                  30
Glu Met Ser Asn Gln Gly Ser Lys Tyr Val Asn Lys Glu Ile Gln Asn
        35                  40                  45
Ala Val Asn Gly Val Lys Gln Ile Lys Thr Leu Ile Glu Lys Thr Asn
    50                  55                  60
Glu Glu Arg Lys Thr Leu Leu Ser Asn Leu Glu Glu Ala Lys Lys Lys
65                  70                  75                  80
Lys Glu Asp Ala Leu Asn Glu Thr Arg Glu Ser Glu Thr Lys Leu Lys
                85                  90                  95
Glu Leu Pro Gly Val Cys Asn Glu Thr Met Met Ala Leu Trp Glu Glu
            100                 105                 110
Cys Lys Pro Cys Leu Lys Gln Thr Cys Met Lys Phe Tyr Ala Arg Val
        115                 120                 125
Cys Arg Ser Gly Ser Gly Leu Val Gly Arg Gln Leu Glu Glu Phe Leu
    130                 135                 140
Asn Gln Ser Ser Pro Phe Tyr Phe Trp Met Asn Gly Asp Arg Ile Asp
145                 150                 155                 160
Ser Leu Leu Glu Asn Asp Arg Gln Gln Thr His Met Leu Asp Val Met
                165                 170                 175
Gln Asp His Phe Ser Arg Ala Ser Ser Ile Ile Asp Glu Leu Phe Gln
            180                 185                 190
Asp Arg Phe Phe Thr Arg Glu Pro Gln Asp Thr Tyr His Tyr Leu Pro
        195                 200                 205
Phe Ser Leu Pro His Arg Arg Pro His Phe Phe Phe Pro Lys Ser Arg
    210                 215                 220
```

```
Ile Val Arg Ser Leu Met Pro Phe Ser Pro Tyr Glu Pro Leu Asn Phe
225                 230                 235                 240
His Ala Met Phe Gln Pro Phe Leu Glu Met Ile His Glu Ala Gln Gln
                245                 250                 255
Ala Met Asp Ile His Phe His Ser Pro Ala Phe Gln His Pro Pro Thr
            260                 265                 270
Glu Phe Ile Arg Glu Gly Asp Asp Asp Arg Thr Val Cys Arg Glu Ile
        275                 280                 285
Arg His Asn Ser Thr Gly Cys Leu Arg Met Lys Asp Gln Cys Asp Lys
    290                 295                 300
Cys Arg Glu Ile Leu Ser Val Asp Cys Ser Thr Asn Asn Pro Ser Gln
305                 310                 315                 320
Ala Lys Leu Arg Arg Glu Leu Asp Glu Ser Leu Gln Val Ala Glu Arg
                325                 330                 335
Leu Thr Arg Lys Tyr Asn Glu Leu Leu Lys Ser Tyr Gln Trp Lys Met
            340                 345                 350
Leu Asn Thr Ser Ser Leu Leu Glu Gln Leu Asn Glu Gln Phe Asn Trp
        355                 360                 365
Val Ser Arg Leu Ala Asn Leu Thr Gln Gly Glu Asp Gln Tyr Tyr Leu
    370                 375                 380
Arg Val Thr Thr Val Ala Ser His Thr Ser Asp Ser Asp Val Pro Ser
385                 390                 395                 400
Gly Val Thr Glu Val Val Val Lys Leu Phe Asp Ser Asp Pro Ile Thr
                405                 410                 415
Val Thr Val Pro Val Glu Val Ser Arg Lys Asn Pro Lys Phe Met Glu
            420                 425                 430
Thr Val Ala Glu Lys Ala Leu Gln Glu Tyr Arg Lys Lys His Arg Glu
        435                 440                 445
Glu
```

<210> 310
<211> 2609
<212> DNA
<213> Homo sapiens

<400> 310

```
ggctctctac ctctcgccgc ccctagggag gacaccatgg gcccactgat ggttcttttt 60
tgcctgctgt tcctgtaccc aggtctggca gactcggctc cctcctgccc tcagaacgtg 120
aatatctcgg gtggcacctt caccctcagc catggctggg ctcctgggag ccttctcacc 180
tactcctgcc cccagggcct gtacccatcc ccagcatcac ggctgtgcaa gagcagcgga 240
cagtggcaga ccccaggagc cacccggtct ctgtctaagg cggtctgcaa acctgtgcgc 300
tgtccagccc ctgtctcctt tgagaatggc atttataccc cacggctggg gtcctatccc 360
gtgggtggca atgtgagctt cgagtgtgag gatggcttca tattgcgggg ctcgcctgtg 420
cgtcagtgtc gccccaacgg catgtgggat ggagaaacag ctgtgtgtga taatggggct 480
ggccactgcc ccaacccagg catttcactg ggcgcagtgc ggacaggctt ccgctttggt 540
catggggaca aggtccgcta tcgctgctcc tcgaatcttg tgctcacggg gtcttcggag 600
cgggagtgcc agggcaacgg ggtctggagt ggaacggagc ccatctgccg ccaaccctac 660
tcttatgact tccctgagga cgtggccccc gccctgggca cttccttctc ccacatgctt 720
ggggccacca atcccaccca gaagacaaag gaaagcctgg gccgtaaaat ccaaatccag 780
cgctctggtc atctgaacct ctacctgctc ctggactgtt cgcagagtgt gtcggaaaat 840
gactttctca tcttcaagga gagcgcctcc ctcatggtgg acaggatctt cagctttgag 900
atcaatgtga gcgttgccat tatcaccttt gcctcagagc ccaaagtcct catgtctgtc 960
ctgaacgaca actcccggga tatgactgag gtgatcagca gcctggaaaa tgccaactat 1020
aaagatcatg aaaatggaac tgggactaac acctatgcag ccttaaacag tgtctatctc 1080
atgatgaaca accaaatgcg actcctcggc atggaaacga tggcctggca ggaaatccga 1140
catgccatca tccttctgac agatggaaag tccaatatgg gtggctctcc caagacagct 1200
```

```
gttgaccata tcagagagat cctgaacatc aaccagaaga ggaatgacta tctggacatc 1260
tatgccatcg gggtgggcaa gctggatgtg gactggagag aactgaatga gctagggtcc 1320
aagaaggatg gtgagaggca tgccttcatt ctgcaggaca caaaggctct gcaccaggtc 1380
tttgaacata tgctggatgt ctccaagctc acagacacca tctgcggggt ggggaacatg 1440
tcagcaaacg cctctgacca ggagaggaca ccctggcatg tcactattaa gcccaagagc 1500
caagagacct gccgggggcc cctcatctcc gaccaatggg tcctgacagc agctcattgc 1560
ttccgcgatg gcaacgacca ctccctgtgg agggtcaatg tgggagaccc caaatcccag 1620
tggggcaaag aattccttat tgagaaggcg gtgatctccc cagggtttga tgtctttgcc 1680
aaaaagaacc agggaatcct ggagttctat ggtgatgaca tagctctgct gaagctggcc 1740
cagaaagtaa agatgtccac ccatgccagg cccatctgcc ttccctgcac gatggaggcc 1800
aatctggctc tgcggagacc tcaaggcagc acctgtaggg accatgagaa tgaactgctg 1860
aacaaacaga gtgttcctgc tcattttgtc gccttgaatg ggagcaaact gaacattaac 1920
cttaagatgg gagtggagtg gacaagctgt gccgaggttg tctcccaaga aaaaaccatg 1980
ttccccaact tgacagatgt cagggaggtg gtgacagacc agttcctatg cagtgggacc 2040
caggaggatg agagtccctg caagggagaa tctgggggag cagttttcct tgagcggaga 2100
ttcaggtttt ttcaggtggg tctggtgagc tggggtcttt acaaccccctg ccttggctct 2160
gctgacaaaa actcccgcaa aagggccct cgtagcaagg tcccgccgcc acgagacttt 2220
cacatcaatc tcttccgcat gcagccctgg ctgaggcagc acctgggggga tgtcctgaat 2280
tttttacccc tctagccatg gccactgagc cctctgctgc cctgccagaa tctgccgccc 2340
ctccatcttc tacctctgaa tggccaccct tagaccctgt gatccatcct ctctcctagc 2400
tgagtaaatc cgggtctcta ggatgccaga ggcagcgcac acaagctggg aaatcctcag 2460
ggctcctacc agcaggactg cctcgctgcc ccacctcccg ctccttggcc tgtccccaga 2520
ttccttccct ggttgacttg actcatgctt gtttcacttt cacatggaat ttcccagtta 2580
tgaaattaat aaaaatcaat ggtttccac                                    2609
```

<210> 311
<211> 752
<212> PRT
<213> Homo sapiens

<400> 311

```
Met Gly Pro Leu Met Val Leu Phe Cys Leu Leu Phe Leu Tyr Pro Gly
 1               5                  10                  15
Leu Ala Asp Ser Ala Pro Ser Cys Pro Gln Asn Val Asn Ile Ser Gly
            20                  25                  30
Gly Thr Phe Thr Leu Ser His Gly Trp Ala Pro Gly Ser Leu Leu Thr
        35                  40                  45
Tyr Ser Cys Pro Gln Gly Leu Tyr Pro Ser Pro Ala Ser Arg Leu Cys
    50                  55                  60
Lys Ser Ser Gly Gln Trp Gln Thr Pro Gly Ala Thr Arg Ser Leu Ser
65                  70                  75                  80
Lys Ala Val Cys Lys Pro Val Arg Cys Pro Ala Pro Val Ser Phe Glu
                85                  90                  95
Asn Gly Ile Tyr Thr Pro Arg Leu Gly Ser Tyr Pro Val Gly Gly Asn
            100                 105                 110
Val Ser Phe Glu Cys Glu Asp Gly Phe Ile Leu Arg Gly Ser Pro Val
        115                 120                 125
Arg Gln Cys Arg Pro Asn Gly Met Trp Asp Gly Glu Thr Ala Val Cys
    130                 135                 140
Asp Asn Gly Ala Gly His Cys Pro Asn Pro Gly Ile Ser Leu Gly Ala
145                 150                 155                 160
Val Arg Thr Gly Phe Arg Phe Gly His Gly Asp Lys Val Arg Tyr Arg
                165                 170                 175
Cys Ser Ser Asn Leu Val Leu Thr Gly Ser Ser Glu Arg Glu Cys Gln
            180                 185                 190
Gly Asn Gly Val Trp Ser Gly Thr Glu Pro Ile Cys Arg Gln Pro Tyr
        195                 200                 205
Ser Tyr Asp Phe Pro Glu Asp Val Ala Pro Ala Leu Gly Thr Ser Phe
```

```
    210                 215                 220
Ser His Met Leu Gly Ala Thr Asn Pro Thr Gln Lys Thr Lys Glu Ser
225                 230                 235                 240
Leu Gly Arg Lys Ile Gln Ile Gln Arg Ser Gly His Leu Asn Leu Tyr
                245                 250                 255
Leu Leu Leu Asp Cys Ser Gln Ser Val Ser Glu Asn Asp Phe Leu Ile
            260                 265                 270
Phe Lys Glu Ser Ala Ser Leu Met Val Asp Arg Ile Phe Ser Phe Glu
        275                 280                 285
Ile Asn Val Ser Val Ala Ile Ile Thr Phe Ala Ser Glu Pro Lys Val
    290                 295                 300
Leu Met Ser Val Leu Asn Asp Asn Ser Arg Asp Met Thr Glu Val Ile
305                 310                 315                 320
Ser Ser Leu Glu Asn Ala Asn Tyr Lys Asp His Glu Asn Gly Thr Gly
                325                 330                 335
Thr Asn Thr Tyr Ala Ala Leu Asn Ser Val Tyr Leu Met Met Asn Asn
            340                 345                 350
Gln Met Arg Leu Leu Gly Met Glu Thr Met Ala Trp Gln Glu Ile Arg
        355                 360                 365
His Ala Ile Ile Leu Leu Thr Asp Gly Lys Ser Asn Met Gly Gly Ser
    370                 375                 380
Pro Lys Thr Ala Val Asp His Ile Arg Glu Ile Leu Asn Ile Asn Gln
385                 390                 395                 400
Lys Arg Asn Asp Tyr Leu Asp Ile Tyr Ala Ile Gly Val Gly Lys Leu
                405                 410                 415
Asp Val Asp Trp Arg Glu Leu Asn Glu Leu Gly Ser Lys Lys Asp Gly
            420                 425                 430
Glu Arg His Ala Phe Ile Leu Gln Asp Thr Lys Ala Leu His Gln Val
        435                 440                 445
Phe Glu His Met Leu Asp Val Ser Lys Leu Thr Asp Thr Ile Cys Gly
    450                 455                 460
Val Gly Asn Met Ser Ala Asn Ala Ser Asp Gln Glu Arg Thr Pro Trp
465                 470                 475                 480
His Val Thr Ile Lys Pro Lys Ser Gln Glu Thr Cys Arg Gly Ala Leu
                485                 490                 495
Ile Ser Asp Gln Trp Val Leu Thr Ala Ala His Cys Phe Arg Asp Gly
            500                 505                 510
Asn Asp His Ser Leu Trp Arg Val Asn Val Gly Asp Pro Lys Ser Gln
        515                 520                 525
Trp Gly Lys Glu Phe Leu Ile Glu Lys Ala Val Ile Ser Pro Gly Phe
    530                 535                 540
Asp Val Phe Ala Lys Lys Asn Gln Gly Ile Leu Glu Phe Tyr Gly Asp
545                 550                 555                 560
Asp Ile Ala Leu Leu Lys Leu Ala Gln Lys Val Lys Met Ser Thr His
                565                 570                 575
Ala Arg Pro Ile Cys Leu Pro Cys Thr Met Glu Ala Asn Leu Ala Leu
            580                 585                 590
Arg Arg Pro Gln Gly Ser Thr Cys Arg Asp His Glu Asn Glu Leu Leu
        595                 600                 605
Asn Lys Gln Ser Val Pro Ala His Phe Val Ala Leu Asn Gly Ser Lys
    610                 615                 620
Leu Asn Ile Asn Leu Lys Met Gly Val Glu Trp Thr Ser Cys Ala Glu
625                 630                 635                 640
Val Val Ser Gln Glu Lys Thr Met Phe Pro Asn Leu Thr Asp Val Arg
                645                 650                 655
Glu Val Val Thr Asp Gln Phe Leu Cys Ser Gly Thr Gln Glu Asp Glu
            660                 665                 670
Ser Pro Cys Lys Gly Glu Ser Gly Gly Ala Val Phe Leu Glu Arg Arg
```

```
        675                 680                 685
Phe Arg Phe Phe Gln Val Gly Leu Val Ser Trp Gly Leu Tyr Asn Pro
    690                 695                 700
Cys Leu Gly Ser Ala Asp Lys Asn Ser Arg Lys Arg Ala Pro Arg Ser
705                 710                 715                 720
Lys Val Pro Pro Pro Arg Asp Phe His Ile Asn Leu Phe Arg Met Gln
                725                 730                 735
Pro Trp Leu Arg Gln His Leu Gly Asp Val Leu Asn Phe Leu Pro Leu
            740                 745                 750
```

<210> 312
<211> 1663
<212> PRT
<213> Homo sapiens

<400> 312

```
Met Gly Pro Thr Ser Gly Pro Ser Leu Leu Leu Leu Leu Leu Thr His
 1               5                  10                  15
Leu Pro Leu Ala Leu Gly Ser Pro Met Tyr Ser Ile Ile Thr Pro Asn
            20                  25                  30
Ile Leu Arg Leu Glu Ser Glu Glu Thr Met Val Leu Glu Ala His Asp
        35                  40                  45
Ala Gln Gly Asp Val Pro Val Thr Val Thr Val His Asp Phe Pro Gly
    50                  55                  60
Lys Lys Leu Val Leu Ser Ser Glu Lys Thr Val Leu Thr Pro Ala Thr
65                  70                  75                  80
Asn His Met Gly Asn Val Thr Phe Thr Ile Pro Ala Asn Arg Glu Phe
                85                  90                  95
Lys Ser Glu Lys Gly Arg Asn Lys Phe Val Thr Val Gln Ala Thr Phe
            100                 105                 110
Gly Thr Gln Val Val Glu Lys Val Val Leu Val Ser Leu Gln Ser Gly
        115                 120                 125
Tyr Leu Phe Ile Gln Thr Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr
    130                 135                 140
Val Leu Tyr Arg Ile Phe Thr Val Asn His Lys Leu Leu Pro Val Gly
145                 150                 155                 160
Arg Thr Val Met Val Asn Ile Glu Asn Pro Glu Gly Ile Pro Val Lys
                165                 170                 175
Gln Asp Ser Leu Ser Ser Gln Asn Gln Leu Gly Val Leu Pro Leu Ser
            180                 185                 190
Trp Asp Ile Pro Glu Leu Val Asn Met Gly Gln Trp Lys Ile Arg Ala
        195                 200                 205
Tyr Tyr Glu Asn Ser Pro Gln Gln Val Phe Ser Thr Glu Phe Glu Val
    210                 215                 220
Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Ile Val Glu Pro Thr Glu
225                 230                 235                 240
Lys Phe Tyr Tyr Ile Tyr Asn Glu Lys Gly Leu Glu Val Thr Ile Thr
                245                 250                 255
Ala Arg Phe Leu Tyr Gly Lys Lys Val Glu Gly Thr Ala Phe Val Ile
            260                 265                 270
Phe Gly Ile Gln Asp Gly Glu Gln Arg Ile Ser Leu Pro Glu Ser Leu
        275                 280                 285
Lys Arg Ile Pro Ile Glu Asp Gly Ser Gly Glu Val Val Leu Ser Arg
    290                 295                 300
Lys Val Leu Leu Asp Gly Val Gln Asn Leu Arg Ala Glu Asp Leu Val
305                 310                 315                 320
Gly Lys Ser Leu Tyr Val Ser Ala Thr Val Ile Leu His Ser Gly Ser
```

```
                    325                 330                 335
Asp Met Val Gln Ala Glu Arg Ser Gly Ile Pro Ile Val Thr Ser Pro
            340                 345                 350
Tyr Gln Ile His Phe Thr Lys Thr Pro Lys Tyr Phe Lys Pro Gly Met
        355                 360                 365
Pro Phe Asp Leu Met Val Phe Val Thr Asn Pro Asp Gly Ser Pro Ala
    370                 375                 380
Tyr Arg Val Pro Val Ala Val Gln Gly Glu Asp Thr Val Gln Ser Leu
385                 390                 395                 400
Thr Gln Gly Asp Gly Val Ala Lys Leu Ser Ile Asn Thr His Pro Ser
                405                 410                 415
Gln Lys Pro Leu Ser Ile Thr Val Arg Thr Lys Lys Gln Glu Leu Ser
            420                 425                 430
Glu Ala Glu Gln Ala Thr Arg Thr Met Gln Ala Leu Pro Tyr Ser Thr
        435                 440                 445
Val Gly Asn Ser Asn Asn Tyr Leu His Leu Ser Val Leu Arg Thr Glu
    450                 455                 460
Leu Arg Pro Gly Glu Thr Leu Asn Val Asn Phe Leu Leu Arg Met Asp
465                 470                 475                 480
Arg Ala His Glu Ala Lys Ile Arg Tyr Tyr Thr Tyr Leu Ile Met Asn
                485                 490                 495
Lys Gly Arg Leu Leu Lys Ala Gly Arg Gln Val Arg Glu Pro Gly Gln
            500                 505                 510
Asp Leu Val Val Leu Pro Leu Ser Ile Thr Thr Asp Phe Ile Pro Ser
        515                 520                 525
Phe Arg Leu Val Ala Tyr Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg
    530                 535                 540
Glu Val Val Ala Asp Ser Val Trp Val Asp Val Lys Asp Ser Cys Val
545                 550                 555                 560
Gly Ser Leu Val Val Lys Ser Gly Gln Ser Glu Asp Arg Gln Pro Val
                565                 570                 575
Pro Gly Gln Gln Met Thr Leu Lys Ile Glu Gly Asp His Gly Ala Arg
            580                 585                 590
Val Val Leu Val Ala Val Asp Lys Gly Val Phe Val Leu Asn Lys Lys
        595                 600                 605
Asn Lys Leu Thr Gln Ser Lys Ile Trp Asp Val Val Glu Lys Ala Asp
    610                 615                 620
Ile Gly Cys Thr Pro Gly Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser
625                 630                 635                 640
Asp Ala Gly Leu Thr Phe Thr Ser Ser Ser Gly Gln Gln Thr Ala Gln
                645                 650                 655
Arg Ala Glu Leu Gln Cys Pro Gln Pro Ala Ala Arg Arg Arg Arg Ser
            660                 665                 670
Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val Gly Lys Tyr Pro Lys
        675                 680                 685
Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met Arg
    690                 695                 700
Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala Cys
705                 710                 715                 720
Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg Arg
                725                 730                 735
Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg Ser Asn Leu Asp
            740                 745                 750
Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg Ser Glu Phe Pro
        755                 760                 765
Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu Pro Pro Lys Asn
    770                 775                 780
Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys Asp Ser Ile Thr
```

785 790 795 800
Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys Lys Gly Ile Cys
805 810 815
Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp Phe Phe Ile Asp
820 825 830
Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln Val Glu Ile Arg
835 840 845
Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu Leu Lys Val Arg Val
850 855 860
Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala Thr Thr Lys Arg
865 870 875 880
Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser Ser Leu Ser Val
885 890 895
Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln Glu Val Glu Val
900 905 910
Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly Val Arg Lys Ser
915 920 925
Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys Thr Val Ala Val
930 935 940
Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly Val Gln Lys Glu
945 950 955 960
Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro Asp Thr Glu Ser
965 970 975
Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala Gln Met Thr Glu
980 985 990
Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile Val Thr Pro Ser
995 1000 1005
Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile Ala
1010 1015 1020
Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu Lys Phe Gly Leu Glu
1025 1030 1035 1040
Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys Gly Tyr Thr Gln Gln
1045 1050 1055
Leu Ala Phe Arg Gln Pro Ser Ser Ala Phe Ala Ala Phe Val Lys Arg
1060 1065 1070
Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val Lys Val Phe Ser Leu
1075 1080 1085
Ala Val Asn Leu Ile Ala Ile Asp Ser Gln Val Leu Cys Gly Ala Val
1090 1095 1100
Lys Trp Leu Ile Leu Glu Lys Gln Lys Pro Asp Gly Val Phe Gln Glu
1105 1110 1115 1120
Asp Ala Pro Val Ile His Gln Glu Met Ile Gly Gly Leu Arg Asn Asn
1125 1130 1135
Asn Glu Lys Asp Met Ala Leu Thr Ala Phe Val Leu Ile Ser Leu Gln
1140 1145 1150
Glu Ala Lys Asp Ile Cys Glu Glu Gln Val Asn Ser Leu Pro Gly Ser
1155 1160 1165
Ile Thr Lys Ala Gly Asp Phe Leu Glu Ala Asn Tyr Met Asn Leu Gln
1170 1175 1180
Arg Ser Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu Ala Gln Met Gly
1185 1190 1195 1200
Arg Leu Lys Gly Pro Leu Leu Asn Lys Phe Leu Thr Thr Ala Lys Asp
1205 1210 1215
Lys Asn Arg Trp Glu Asp Pro Gly Lys Gln Leu Tyr Asn Val Glu Ala
1220 1225 1230
Thr Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu Lys Asp Phe Asp Phe
1235 1240 1245
Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg Tyr Tyr Gly Gly

```
    1250                1255                1260
Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln Ala Leu Ala
1265                1270                1275                1280
Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu Leu Asn Leu Asp Val
                1285                1290                1295
Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile Thr His Arg Ile His
            1300                1305                1310
Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu Thr Lys Glu Asn Glu
        1315                1320                1325
Gly Phe Thr Val Thr Ala Glu Gly Lys Gly Gln Gly Thr Leu Ser Val
    1330                1335                1340
Val Thr Met Tyr His Ala Lys Ala Lys Asp Gln Leu Thr Cys Asn Lys
1345                1350                1355                1360
Phe Asp Leu Lys Val Thr Ile Lys Pro Ala Pro Glu Thr Glu Lys Arg
                1365                1370                1375
Pro Gln Asp Ala Lys Asn Thr Met Ile Leu Glu Ile Cys Thr Arg Tyr
            1380                1385                1390
Arg Gly Asp Gln Asp Ala Thr Met Ser Ile Leu Asp Ile Ser Met Met
        1395                1400                1405
Thr Gly Phe Ala Pro Asp Thr Asp Asp Leu Lys Gln Leu Ala Asn Gly
    1410                1415                1420
Val Asp Arg Tyr Ile Ser Lys Tyr Glu Leu Asp Lys Ala Phe Ser Asp
1425                1430                1435                1440
Arg Asn Thr Leu Ile Ile Tyr Leu Asp Lys Val Ser His Ser Glu Asp
                1445                1450                1455
Asp Cys Leu Ala Phe Lys Val His Gln Tyr Phe Asn Val Glu Leu Ile
            1460                1465                1470
Gln Pro Gly Ala Val Lys Val Tyr Ala Tyr Tyr Asn Leu Glu Glu Ser
        1475                1480                1485
Cys Thr Arg Phe Tyr His Pro Glu Lys Glu Asp Gly Lys Leu Asn Lys
    1490                1495                1500
Leu Cys Arg Asp Glu Leu Cys Arg Cys Ala Glu Glu Asn Cys Phe Ile
1505                1510                1515                1520
Gln Lys Ser Asp Asp Lys Val Thr Leu Glu Glu Arg Leu Asp Lys Ala
                1525                1530                1535
Cys Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr Arg Leu Val Lys Val
            1540                1545                1550
Gln Leu Ser Asn Asp Phe Asp Glu Tyr Ile Met Ala Ile Glu Gln Thr
        1555                1560                1565
Ile Lys Ser Gly Ser Asp Glu Val Gln Val Gly Gln Gln Arg Thr Phe
    1570                1575                1580
Ile Ser Pro Ile Lys Cys Arg Glu Ala Leu Lys Leu Glu Glu Lys Lys
1585                1590                1595                1600
His Tyr Leu Met Trp Gly Leu Ser Ser Asp Phe Trp Gly Glu Lys Pro
                1605                1610                1615
Asn Leu Ser Tyr Ile Ile Gly Lys Asp Thr Trp Val Glu His Trp Pro
            1620                1625                1630
Glu Glu Asp Glu Cys Gln Asp Glu Glu Asn Gln Lys Gln Cys Gln Asp
        1635                1640                1645
Leu Gly Ala Phe Thr Glu Ser Met Val Val Phe Gly Cys Pro Asn
    1650                1655                1660
```

<210> 313
<211> 1744
<212> PRT
<213> Homo sapiens

<400> 313

```
Met Arg Leu Leu Trp Gly Leu Ile Trp Ala Ser Ser Phe Phe Thr Leu
 1               5                  10                  15
Ser Leu Gln Lys Pro Arg Leu Leu Leu Phe Ser Pro Ser Val Val His
            20                  25                  30
Leu Gly Val Pro Leu Ser Val Gly Val Gln Leu Gln Asp Val Pro Arg
        35                  40                  45
Gly Gln Val Val Lys Gly Ser Val Phe Leu Arg Asn Pro Ser Arg Asn
    50                  55                  60
Asn Val Pro Cys Ser Pro Lys Val Asp Phe Thr Leu Ser Ser Glu Arg
65                  70                  75                  80
Asp Phe Ala Leu Leu Ser Leu Gln Val Pro Leu Lys Asp Ala Lys Ser
                85                  90                  95
Cys Gly Leu His Gln Leu Leu Arg Gly Pro Glu Val Gln Leu Val Ala
            100                 105                 110
His Ser Pro Trp Leu Lys Asp Ser Leu Ser Arg Thr Thr Asn Ile Gln
        115                 120                 125
Gly Ile Asn Leu Leu Phe Ser Ser Arg Arg Gly His Leu Phe Leu Gln
    130                 135                 140
Thr Asp Gln Pro Ile Tyr Asn Pro Gly Gln Arg Val Arg Tyr Arg Val
145                 150                 155                 160
Phe Ala Leu Asp Gln Lys Met Arg Pro Ser Thr Asp Thr Ile Thr Val
                165                 170                 175
Met Val Glu Asn Ser His Gly Leu Arg Val Arg Lys Lys Glu Val Tyr
            180                 185                 190
Met Pro Ser Ser Ile Phe Gln Asp Asp Phe Val Ile Pro Asp Ile Ser
        195                 200                 205
Glu Pro Gly Thr Trp Lys Ile Ser Ala Arg Phe Ser Asp Gly Leu Glu
    210                 215                 220
Ser Asn Ser Ser Thr Gln Phe Glu Val Lys Lys Tyr Val Leu Pro Asn
225                 230                 235                 240
Phe Glu Val Lys Ile Thr Pro Gly Lys Pro Tyr Ile Leu Thr Val Pro
                245                 250                 255
Gly His Leu Asp Glu Met Gln Leu Asp Ile Gln Ala Arg Tyr Ile Tyr
            260                 265                 270
Gly Lys Pro Val Gln Gly Val Ala Tyr Val Arg Phe Gly Leu Leu Asp
        275                 280                 285
Glu Asp Gly Lys Lys Thr Phe Phe Arg Gly Leu Glu Ser Gln Thr Lys
    290                 295                 300
Leu Val Asn Gly Gln Ser His Ile Ser Leu Ser Lys Ala Glu Phe Gln
305                 310                 315                 320
Asp Ala Leu Glu Lys Leu Asn Met Gly Ile Thr Asp Leu Gln Gly Leu
                325                 330                 335
Arg Leu Tyr Val Ala Ala Ala Ile Ile Glu Ser Pro Gly Gly Glu Met
            340                 345                 350
Glu Glu Ala Glu Leu Thr Ser Trp Tyr Phe Val Ser Ser Pro Phe Ser
        355                 360                 365
Leu Asp Leu Ser Lys Thr Lys Arg His Leu Val Pro Gly Ala Pro Phe
    370                 375                 380
Leu Leu Gln Ala Leu Val Arg Glu Met Ser Gly Ser Pro Ala Ser Gly
385                 390                 395                 400
Ile Pro Val Lys Val Ser Ala Thr Val Ser Ser Pro Gly Ser Val Pro
                405                 410                 415
Glu Val Gln Asp Ile Gln Gln Asn Thr Asp Gly Ser Gly Gln Val Ser
            420                 425                 430
Ile Pro Ile Ile Ile Pro Gln Thr Ile Ser Glu Leu Gln Leu Ser Val
        435                 440                 445
Ser Ala Gly Ser Pro His Pro Ala Ile Ala Arg Leu Thr Val Ala Ala
```

```
    450                 455                 460
Pro Pro Ser Gly Gly Pro Gly Phe Leu Ser Ile Glu Arg Pro Asp Ser
465                 470                 475                 480
Arg Pro Pro Arg Val Gly Asp Thr Leu Asn Leu Asn Leu Arg Ala Val
                485                 490                 495
Gly Ser Gly Ala Thr Phe Ser His Tyr Tyr Tyr Met Ile Leu Ser Arg
            500                 505                 510
Gly Gln Ile Val Phe Met Asn Arg Glu Pro Lys Arg Thr Leu Thr Ser
        515                 520                 525
Val Ser Val Phe Val Asp His His Leu Ala Pro Ser Phe Tyr Phe Val
    530                 535                 540
Ala Phe Tyr Tyr His Gly Asp His Pro Val Ala Asn Ser Leu Arg Val
545                 550                 555                 560
Asp Val Gln Ala Gly Ala Cys Glu Gly Lys Leu Glu Leu Ser Val Asp
                565                 570                 575
Gly Ala Lys Gln Tyr Arg Asn Gly Glu Ser Val Lys Leu His Leu Glu
            580                 585                 590
Thr Asp Ser Leu Ala Leu Val Ala Leu Gly Ala Leu Asp Thr Ala Leu
        595                 600                 605
Tyr Ala Ala Gly Ser Lys Ser His Lys Pro Leu Asn Met Gly Lys Val
    610                 615                 620
Phe Glu Ala Met Asn Ser Tyr Asp Leu Gly Cys Gly Pro Gly Gly Gly
625                 630                 635                 640
Asp Ser Ala Leu Gln Val Phe Gln Ala Ala Gly Leu Ala Phe Ser Asp
                645                 650                 655
Gly Asp Gln Trp Thr Leu Ser Arg Lys Arg Leu Ser Cys Pro Lys Glu
            660                 665                 670
Lys Thr Thr Arg Lys Lys Arg Asn Val Asn Phe Gln Lys Ala Ile Asn
        675                 680                 685
Glu Lys Leu Gly Gln Tyr Ala Ser Pro Thr Ala Lys Arg Cys Cys Gln
    690                 695                 700
Asp Gly Val Thr Arg Leu Pro Met Met Arg Ser Cys Glu Gln Arg Ala
705                 710                 715                 720
Ala Arg Val Gln Gln Pro Asp Cys Arg Glu Pro Phe Leu Ser Cys Cys
                725                 730                 735
Gln Phe Ala Glu Ser Leu Arg Lys Lys Ser Arg Asp Lys Gly Gln Ala
            740                 745                 750
Gly Leu Gln Arg Ala Leu Glu Ile Leu Gln Glu Glu Asp Leu Ile Asp
        755                 760                 765
Glu Asp Asp Ile Pro Val Arg Ser Phe Phe Pro Glu Asn Trp Leu Trp
    770                 775                 780
Arg Val Glu Thr Val Asp Arg Phe Gln Ile Leu Thr Leu Trp Leu Pro
785                 790                 795                 800
Asp Ser Leu Thr Thr Trp Glu Ile His Gly Leu Ser Leu Ser Lys Thr
                805                 810                 815
Lys Gly Leu Cys Val Ala Thr Pro Val Gln Leu Arg Val Phe Arg Glu
            820                 825                 830
Phe His Leu His Leu Arg Leu Pro Met Ser Val Arg Arg Phe Glu Gln
        835                 840                 845
Leu Glu Leu Arg Pro Val Leu Tyr Asn Tyr Leu Asp Lys Asn Leu Thr
    850                 855                 860
Val Ser Val His Val Ser Pro Val Glu Gly Leu Cys Leu Ala Gly Gly
865                 870                 875                 880
Gly Gly Leu Ala Gln Gln Val Leu Val Pro Ala Gly Ser Ala Arg Pro
                885                 890                 895
Val Ala Phe Ser Val Val Pro Thr Ala Ala Ala Ala Val Ser Leu Lys
            900                 905                 910
Val Val Ala Arg Gly Ser Phe Glu Phe Pro Val Gly Asp Ala Val Ser
```

915 920 925
Lys Val Leu Gln Ile Glu Lys Glu Gly Ala Ile His Arg Glu Glu Leu
930 935 940
Val Tyr Glu Leu Asn Pro Leu Asp His Arg Gly Arg Thr Leu Glu Ile
945 950 955 960
Pro Gly Asn Ser Asp Pro Asn Met Ile Pro Asp Gly Asp Phe Asn Ser
965 970 975
Tyr Val Arg Val Thr Ala Ser Asp Pro Leu Asp Thr Leu Gly Ser Glu
980 985 990
Gly Ala Leu Ser Pro Gly Gly Val Ala Ser Leu Leu Arg Leu Pro Arg
995 1000 1005
Gly Cys Gly Glu Gln Thr Met Ile Tyr Leu Ala Pro Thr Leu Ala Ala
1010 1015 1020
Ser Arg Tyr Leu Asp Lys Thr Glu Gln Trp Ser Thr Leu Pro Pro Glu
1025 1030 1035 1040
Thr Lys Asp His Ala Val Asp Leu Ile Gln Lys Gly Tyr Met Arg Ile
1045 1050 1055
Gln Gln Phe Arg Lys Ala Asp Gly Ser Tyr Ala Ala Trp Leu Ser Arg
1060 1065 1070
Asp Ser Ser Thr Trp Leu Thr Ala Phe Val Leu Lys Val Leu Ser Leu
1075 1080 1085
Ala Gln Glu Gln Val Gly Gly Ser Pro Glu Lys Leu Gln Glu Thr Ser
1090 1095 1100
Asn Trp Leu Leu Ser Gln Gln Gln Ala Asp Gly Ser Phe Gln Asp Pro
1105 1110 1115 1120
Cys Pro Val Leu Asp Arg Ser Met Gln Gly Gly Leu Val Gly Asn Asp
1125 1130 1135
Glu Thr Val Ala Leu Thr Ala Phe Val Thr Ile Ala Leu His His Gly
1140 1145 1150
Leu Ala Val Phe Gln Asp Glu Gly Ala Glu Pro Leu Lys Gln Arg Val
1155 1160 1165
Glu Ala Ser Ile Ser Lys Ala Asn Ser Phe Leu Gly Glu Lys Ala Ser
1170 1175 1180
Ala Gly Leu Leu Gly Ala His Ala Ala Ala Ile Thr Ala Tyr Ala Leu
1185 1190 1195 1200
Ser Leu Thr Lys Ala Pro Val Asp Leu Leu Gly Val Ala His Asn Asn
1205 1210 1215
Leu Met Ala Met Ala Gln Glu Thr Gly Asp Asn Leu Tyr Trp Gly Ser
1220 1225 1230
Val Thr Gly Ser Gln Ser Asn Ala Val Ser Pro Thr Pro Ala Pro Arg
1235 1240 1245
Asn Pro Ser Asp Pro Met Pro Gln Ala Pro Ala Leu Trp Ile Glu Thr
1250 1255 1260
Thr Ala Tyr Ala Leu Leu His Leu Leu Leu His Glu Gly Lys Ala Glu
1265 1270 1275 1280
Met Ala Asp Gln Ala Ser Ala Trp Leu Thr Arg Gln Gly Ser Phe Gln
1285 1290 1295
Gly Gly Phe Arg Ser Thr Gln Asp Thr Val Ile Ala Leu Asp Ala Leu
1300 1305 1310
Ser Ala Tyr Trp Ile Ala Ser His Thr Thr Glu Glu Arg Gly Leu Asn
1315 1320 1325
Val Thr Leu Ser Ser Thr Gly Arg Asn Gly Phe Lys Ser His Ala Leu
1330 1335 1340
Gln Leu Asn Asn Arg Gln Ile Arg Gly Leu Glu Glu Glu Leu Gln Phe
1345 1350 1355 1360
Ser Leu Gly Ser Lys Ile Asn Val Lys Val Gly Gly Asn Ser Lys Gly
1365 1370 1375
Thr Leu Lys Val Leu Arg Thr Tyr Asn Val Leu Asp Met Lys Asn Thr

```
            1380                1385                1390
Thr Cys Gln Asp Leu Gln Ile Glu Val Thr Val Lys Gly His Val Glu
        1395                1400                1405
Tyr Thr Met Glu Ala Asn Glu Asp Tyr Glu Asp Tyr Glu Tyr Asp Glu
    1410                1415                1420
Leu Pro Ala Lys Asp Asp Pro Asp Ala Pro Leu Gln Pro Val Thr Pro
1425                1430                1435                1440
Leu Gln Leu Phe Glu Gly Arg Arg Asn Arg Arg Arg Arg Glu Ala Pro
                1445                1450                1455
Lys Val Val Glu Glu Gln Glu Ser Arg Val His Tyr Thr Val Cys Ile
            1460                1465                1470
Trp Arg Asn Gly Lys Val Gly Leu Ser Gly Met Ala Ile Ala Asp Val
        1475                1480                1485
Thr Leu Leu Ser Gly Phe His Ala Leu Arg Ala Asp Leu Glu Lys Leu
    1490                1495                1500
Thr Ser Leu Ser Asp Arg Tyr Val Ser His Phe Glu Thr Glu Gly Pro
1505                1510                1515                1520
His Val Leu Leu Tyr Phe Asp Ser Val Pro Thr Ser Arg Glu Cys Val
                1525                1530                1535
Gly Phe Glu Ala Val Gln Glu Val Pro Val Gly Leu Val Gln Pro Ala
            1540                1545                1550
Ser Ala Thr Leu Tyr Asp Tyr Tyr Asn Pro Glu Arg Arg Cys Ser Val
        1555                1560                1565
Phe Tyr Gly Ala Pro Ser Lys Ser Arg Leu Leu Ala Thr Leu Cys Ser
    1570                1575                1580
Ala Glu Val Cys Gln Cys Ala Glu Gly Lys Cys Pro Arg Gln Arg Arg
1585                1590                1595                1600
Ala Leu Glu Arg Gly Leu Gln Asp Glu Asp Gly Tyr Arg Met Lys Phe
                1605                1610                1615
Ala Cys Tyr Tyr Pro Arg Val Glu Tyr Gly Phe Gln Val Lys Val Leu
            1620                1625                1630
Arg Glu Asp Ser Arg Ala Ala Phe Arg Leu Phe Glu Thr Lys Ile Thr
        1635                1640                1645
Gln Val Leu His Phe Thr Lys Asp Val Lys Ala Ala Ala Asn Gln Met
    1650                1655                1660
Arg Asn Phe Leu Val Arg Ala Ser Cys Arg Leu Arg Leu Glu Pro Gly
1665                1670                1675                1680
Lys Glu Tyr Leu Ile Met Gly Leu Asp Gly Ala Thr Tyr Asp Leu Glu
                1685                1690                1695
Gly His Pro Gln Tyr Leu Leu Asp Ser Asn Ser Trp Ile Glu Glu Met
            1700                1705                1710
Pro Ser Glu Arg Leu Cys Arg Ser Thr Arg Gln Arg Ala Ala Cys Ala
        1715                1720                1725
Gln Leu Asn Asp Phe Leu Gln Glu Tyr Gly Thr Gln Gly Cys Gln Val
    1730                1735                1740
```

<210> 314
<211> 1676
<212> PRT
<213> Homo sapiens

<400> 314

```
Met Gly Leu Leu Gly Ile Leu Cys Phe Leu Ile Phe Leu Gly Lys Thr
 1               5                  10                  15
Trp Gly Gln Glu Gln Thr Tyr Val Ile Ser Ala Pro Lys Ile Phe Arg
            20                  25                  30
Val Gly Ala Ser Glu Asn Ile Val Ile Gln Val Tyr Gly Tyr Thr Glu
```

```
          35                  40                  45
Ala Phe Asp Ala Thr Ile Ser Ile Lys Ser Tyr Pro Asp Lys Lys Phe
     50                  55                  60
Ser Tyr Ser Ser Gly His Val His Leu Ser Ser Glu Asn Lys Phe Gln
65                  70                  75                  80
Asn Ser Ala Ile Leu Thr Ile Gln Pro Lys Gln Leu Pro Gly Gly Gln
                85                  90                  95
Asn Pro Val Ser Tyr Val Tyr Leu Glu Val Val Ser Lys His Phe Ser
            100                 105                 110
Lys Ser Lys Arg Met Pro Ile Thr Tyr Asp Asn Gly Phe Leu Phe Ile
        115                 120                 125
His Thr Asp Lys Pro Val Tyr Thr Pro Asp Gln Ser Val Lys Val Arg
    130                 135                 140
Val Tyr Ser Leu Asn Asp Asp Leu Lys Pro Ala Lys Arg Glu Thr Val
145                 150                 155                 160
Leu Thr Phe Ile Asp Pro Glu Gly Ser Glu Val Asp Met Val Glu Glu
                165                 170                 175
Ile Asp His Ile Gly Ile Ile Ser Phe Pro Asp Phe Lys Ile Pro Ser
            180                 185                 190
Asn Pro Arg Tyr Gly Met Trp Thr Ile Lys Ala Lys Tyr Lys Glu Asp
        195                 200                 205
Phe Ser Thr Thr Gly Thr Ala Tyr Phe Glu Val Lys Glu Tyr Val Leu
    210                 215                 220
Pro His Phe Ser Val Ser Ile Glu Pro Glu Tyr Asn Phe Ile Gly Tyr
225                 230                 235                 240
Lys Asn Phe Lys Asn Phe Glu Ile Thr Ile Lys Ala Arg Tyr Phe Tyr
                245                 250                 255
Asn Lys Val Val Thr Glu Ala Asp Val Tyr Ile Thr Phe Gly Ile Arg
            260                 265                 270
Glu Asp Leu Lys Asp Asp Gln Lys Glu Met Met Gln Thr Ala Met Gln
        275                 280                 285
Asn Thr Met Leu Ile Asn Gly Ile Ala Gln Val Thr Phe Asp Ser Glu
    290                 295                 300
Thr Ala Val Lys Glu Leu Ser Tyr Tyr Ser Leu Glu Asp Leu Asn Asn
305                 310                 315                 320
Lys Tyr Leu Tyr Ile Ala Val Thr Val Ile Glu Ser Thr Gly Gly Phe
                325                 330                 335
Ser Glu Glu Ala Glu Ile Pro Gly Ile Lys Tyr Val Leu Ser Pro Tyr
            340                 345                 350
Lys Leu Asn Leu Val Ala Thr Pro Leu Phe Leu Lys Pro Gly Ile Pro
        355                 360                 365
Tyr Pro Ile Lys Val Gln Val Lys Asp Ser Leu Asp Gln Leu Val Gly
    370                 375                 380
Gly Val Pro Val Ile Leu Asn Ala Gln Thr Ile Asp Val Asn Gln Glu
385                 390                 395                 400
Thr Ser Asp Leu Asp Pro Ser Lys Ser Val Thr Arg Val Asp Asp Gly
                405                 410                 415
Val Ala Ser Phe Val Leu Asn Leu Pro Ser Gly Val Thr Val Leu Glu
            420                 425                 430
Phe Asn Val Lys Thr Asp Ala Pro Asp Leu Pro Glu Glu Asn Gln Ala
        435                 440                 445
Arg Glu Gly Tyr Arg Ala Ile Ala Tyr Ser Ser Leu Ser Gln Ser Tyr
    450                 455                 460
Leu Tyr Ile Asp Trp Thr Asp Asn His Lys Ala Leu Leu Val Gly Glu
465                 470                 475                 480
His Leu Asn Ile Ile Val Thr Pro Lys Ser Pro Tyr Ile Asp Lys Ile
                485                 490                 495
Thr His Tyr Asn Tyr Leu Ile Leu Ser Lys Gly Lys Ile Ile His Phe
```

```
                500                 505                 510
Gly Thr Arg Glu Lys Phe Ser Asp Ala Ser Tyr Gln Ser Ile Asn Ile
            515                 520                 525
Pro Val Thr Gln Asn Met Val Pro Ser Ser Arg Leu Leu Val Tyr Tyr
        530                 535                 540
Ile Val Thr Gly Glu Gln Thr Ala Glu Leu Val Ser Asp Ser Val Trp
545                 550                 555                 560
Leu Asn Ile Glu Glu Lys Cys Gly Asn Gln Leu Gln Val His Leu Ser
                565                 570                 575
Pro Asp Ala Asp Ala Tyr Ser Pro Gly Gln Thr Val Ser Leu Asn Met
            580                 585                 590
Ala Thr Gly Met Asp Ser Trp Val Ala Leu Ala Ala Val Asp Ser Ala
        595                 600                 605
Val Tyr Gly Val Gln Arg Gly Ala Lys Lys Pro Leu Glu Arg Val Phe
    610                 615                 620
Gln Phe Leu Glu Lys Ser Asp Leu Gly Cys Gly Ala Gly Gly Gly Leu
625                 630                 635                 640
Asn Asn Ala Asn Val Phe His Leu Ala Gly Leu Thr Phe Leu Thr Asn
                645                 650                 655
Ala Asn Ala Asp Asp Ser Gln Glu Asn Asp Glu Pro Cys Lys Glu Ile
            660                 665                 670
Leu Arg Pro Arg Arg Thr Leu Gln Lys Lys Ile Glu Glu Ile Ala Ala
        675                 680                 685
Lys Tyr Lys His Ser Val Val Lys Lys Cys Cys Tyr Asp Gly Ala Cys
    690                 695                 700
Val Asn Asn Asp Glu Thr Cys Glu Gln Arg Ala Ala Arg Ile Ser Leu
705                 710                 715                 720
Gly Pro Arg Cys Ile Lys Ala Phe Thr Glu Cys Cys Val Val Ala Ser
                725                 730                 735
Gln Leu Arg Ala Asn Ile Ser His Lys Asp Met Gln Leu Gly Arg Leu
            740                 745                 750
His Met Lys Thr Leu Leu Pro Val Ser Lys Pro Glu Ile Arg Ser Tyr
        755                 760                 765
Phe Pro Glu Ser Trp Leu Trp Glu Val His Leu Val Pro Arg Arg Lys
    770                 775                 780
Gln Leu Gln Phe Ala Leu Pro Asp Ser Leu Thr Thr Trp Glu Ile Gln
785                 790                 795                 800
Gly Ile Gly Ile Ser Asn Thr Gly Ile Cys Val Ala Asp Thr Val Lys
                805                 810                 815
Ala Lys Val Phe Lys Asp Val Phe Leu Glu Met Asn Ile Pro Tyr Ser
            820                 825                 830
Val Val Arg Gly Glu Gln Ile Gln Leu Lys Gly Thr Val Tyr Asn Tyr
        835                 840                 845
Arg Thr Ser Gly Met Gln Phe Cys Val Lys Met Ser Ala Val Glu Gly
    850                 855                 860
Ile Cys Thr Ser Glu Ser Pro Val Ile Asp His Gln Gly Thr Lys Ser
865                 870                 875                 880
Ser Lys Cys Val Arg Gln Lys Val Glu Gly Ser Ser Ser His Leu Val
                885                 890                 895
Thr Phe Thr Val Leu Pro Leu Glu Ile Gly Leu His Asn Ile Asn Phe
            900                 905                 910
Ser Leu Glu Thr Trp Phe Gly Lys Glu Ile Leu Val Lys Thr Leu Arg
        915                 920                 925
Val Val Pro Glu Gly Val Lys Arg Glu Ser Tyr Ser Gly Val Thr Leu
    930                 935                 940
Asp Pro Arg Gly Ile Tyr Gly Thr Ile Ser Arg Arg Lys Glu Phe Pro
945                 950                 955                 960
Tyr Arg Ile Pro Leu Asp Leu Val Pro Lys Thr Glu Ile Lys Arg Ile
```

965 970 975
Leu Ser Val Lys Gly Leu Leu Val Gly Glu Ile Leu Ser Ala Val Leu
980 985 990
Ser Gln Glu Gly Ile Asn Ile Leu Thr His Leu Pro Lys Gly Ser Ala
995 1000 1005
Glu Ala Glu Leu Met Ser Val Val Pro Val Phe Tyr Val Phe His Tyr
1010 1015 1020
Leu Glu Thr Gly Asn His Trp Asn Ile Phe His Ser Asp Pro Leu Ile
1025 1030 1035 1040
Glu Lys Gln Lys Leu Lys Lys Lys Leu Lys Glu Gly Met Leu Ser Ile
1045 1050 1055
Met Ser Tyr Arg Asn Ala Asp Tyr Ser Tyr Ser Val Trp Lys Gly Gly
1060 1065 1070
Ser Ala Ser Thr Trp Leu Thr Ala Phe Ala Leu Arg Val Leu Gly Gln
1075 1080 1085
Val Asn Lys Tyr Val Glu Gln Asn Gln Asn Ser Ile Cys Asn Ser Leu
1090 1095 1100
Leu Trp Leu Val Glu Asn Tyr Gln Leu Asp Asn Gly Ser Phe Lys Glu
1105 1110 1115 1120
Asn Ser Gln Tyr Gln Pro Ile Lys Leu Gln Gly Thr Leu Pro Val Glu
1125 1130 1135
Ala Arg Glu Asn Ser Leu Tyr Leu Thr Ala Phe Thr Val Ile Gly Ile
1140 1145 1150
Arg Lys Ala Phe Asp Ile Cys Pro Leu Val Lys Ile Asp Thr Ala Leu
1155 1160 1165
Ile Lys Ala Asp Asn Phe Leu Leu Glu Asn Thr Leu Pro Ala Gln Ser
1170 1175 1180
Thr Phe Thr Leu Ala Ile Ser Ala Tyr Ala Leu Ser Leu Gly Asp Lys
1185 1190 1195 1200
Thr His Pro Gln Phe Arg Ser Ile Val Ser Ala Leu Lys Arg Glu Ala
1205 1210 1215
Leu Val Lys Gly Asn Pro Pro Ile Tyr Arg Phe Trp Lys Asp Asn Leu
1220 1225 1230
Gln His Lys Asp Ser Ser Val Pro Asn Thr Gly Thr Ala Arg Met Val
1235 1240 1245
Glu Thr Thr Ala Tyr Ala Leu Leu Thr Ser Leu Asn Leu Lys Asp Ile
1250 1255 1260
Asn Tyr Val Asn Pro Val Ile Lys Trp Leu Ser Glu Glu Gln Arg Tyr
1265 1270 1275 1280
Gly Gly Gly Phe Tyr Ser Thr Gln Asp Thr Ile Asn Ala Ile Glu Gly
1285 1290 1295
Leu Thr Glu Tyr Ser Leu Leu Val Lys Gln Leu Arg Leu Ser Met Asp
1300 1305 1310
Ile Asp Val Ser Tyr Lys His Lys Gly Ala Leu His Asn Tyr Lys Met
1315 1320 1325
Thr Asp Lys Asn Phe Leu Gly Arg Pro Val Glu Val Leu Leu Asn Asp
1330 1335 1340
Asp Leu Ile Val Ser Thr Gly Phe Gly Ser Gly Leu Ala Thr Val His
1345 1350 1355 1360
Val Thr Thr Val Val His Lys Thr Ser Thr Ser Glu Glu Val Cys Ser
1365 1370 1375
Phe Tyr Leu Lys Ile Asp Thr Gln Asp Ile Glu Ala Ser His Tyr Arg
1380 1385 1390
Gly Tyr Gly Asn Ser Asp Tyr Lys Arg Ile Val Ala Cys Ala Ser Tyr
1395 1400 1405
Lys Pro Ser Arg Glu Glu Ser Ser Ser Gly Ser Ser His Ala Val Met
1410 1415 1420
Asp Ile Ser Leu Pro Thr Gly Ile Ser Ala Asn Glu Glu Asp Leu Lys

1425 1430 1435 1440
Ala Leu Val Glu Gly Val Asp Gln Leu Phe Thr Asp Tyr Gln Ile Lys
1445 1450 1455
Asp Gly His Val Ile Leu Gln Leu Asn Ser Ile Pro Ser Ser Asp Phe
1460 1465 1470
Leu Cys Val Arg Phe Arg Ile Phe Glu Leu Phe Glu Val Gly Phe Leu
1475 1480 1485
Ser Pro Ala Thr Phe Thr Val Tyr Glu Tyr His Arg Pro Asp Lys Gln
1490 1495 1500
Cys Thr Met Phe Tyr Ser Thr Ser Asn Ile Lys Ile Gln Lys Val Cys
1505 1510 1515 1520
Glu Gly Ala Ala Cys Lys Cys Val Glu Ala Asp Cys Gly Gln Met Gln
1525 1530 1535
Glu Glu Leu Asp Leu Thr Ile Ser Ala Glu Thr Arg Lys Gln Thr Ala
1540 1545 1550
Cys Lys Pro Glu Ile Ala Tyr Ala Tyr Lys Val Ser Ile Thr Ser Ile
1555 1560 1565
Thr Val Glu Asn Val Phe Val Lys Tyr Lys Ala Thr Leu Leu Asp Ile
1570 1575 1580
Tyr Lys Thr Gly Glu Ala Val Ala Glu Lys Asp Ser Glu Ile Thr Phe
1585 1590 1595 1600
Ile Lys Lys Val Thr Cys Thr Asn Ala Glu Leu Val Lys Gly Arg Gln
1605 1610 1615
Tyr Leu Ile Met Gly Lys Glu Ala Leu Gln Ile Lys Tyr Asn Phe Ser
1620 1625 1630
Phe Arg Tyr Ile Tyr Pro Leu Asp Ser Leu Thr Trp Ile Glu Tyr Trp
1635 1640 1645
Pro Arg Asp Thr Thr Cys Ser Ser Cys Gln Ala Phe Leu Ala Asn Leu
1650 1655 1660
Asp Glu Phe Ala Glu Asp Ile Phe Leu Asn Gly Cys
1665 1670 1675

<210> 315
<211> 934
<212> PRT
<213> Homo sapiens

<400> 315
Met Ala Arg Arg Ser Val Leu Tyr Phe Ile Leu Leu Asn Ala Leu Ile
1 5 10 15
Asn Lys Gly Gln Ala Cys Phe Cys Asp His Tyr Ala Trp Thr Gln Trp
20 25 30
Thr Ser Cys Ser Lys Thr Cys Asn Ser Gly Thr Gln Ser Arg His Arg
35 40 45
Gln Ile Val Val Asp Lys Tyr Tyr Gln Glu Asn Phe Cys Glu Gln Ile
50 55 60
Cys Ser Lys Gln Glu Thr Arg Glu Cys Asn Trp Gln Arg Cys Pro Ile
65 70 75 80
Asn Cys Leu Leu Gly Asp Phe Gly Pro Trp Ser Asp Cys Asp Pro Cys
85 90 95
Ile Glu Lys Gln Ser Lys Val Arg Ser Val Leu Arg Pro Ser Gln Phe
100 105 110
Gly Gly Gln Pro Cys Thr Glu Pro Leu Val Ala Phe Gln Pro Cys Ile
115 120 125
Pro Ser Lys Leu Cys Lys Ile Glu Glu Ala Asp Cys Lys Asn Lys Phe
130 135 140
Arg Cys Asp Ser Gly Arg Cys Ile Ala Arg Lys Leu Glu Cys Asn Gly

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145                 150                 155                 160
Glu Asn Asp Cys Gly Asp Asn Ser Asp Glu Arg Asp Cys Gly Arg Thr
                165                 170                 175
Lys Ala Val Cys Thr Arg Lys Tyr Asn Pro Ile Pro Ser Val Gln Leu
            180                 185                 190
Met Gly Asn Gly Phe His Phe Leu Ala Gly Glu Pro Arg Gly Glu Val
        195                 200                 205
Leu Asp Asn Ser Phe Thr Gly Gly Ile Cys Lys Thr Val Lys Ser Ser
    210                 215                 220
Arg Thr Ser Asn Pro Tyr Arg Val Pro Ala Asn Leu Glu Asn Val Gly
225                 230                 235                 240
Phe Glu Val Gln Thr Ala Glu Asp Asp Leu Lys Thr Asp Phe Tyr Lys
                245                 250                 255
Asp Leu Thr Ser Leu Gly His Asn Glu Asn Gln Gln Gly Ser Phe Ser
            260                 265                 270
Ser Gln Gly Gly Ser Ser Phe Ser Val Pro Ile Phe Tyr Ser Ser Lys
        275                 280                 285
Arg Ser Glu Asn Ile Asn His Asn Ser Ala Phe Lys Gln Ala Ile Gln
    290                 295                 300
Ala Ser His Lys Lys Asp Ser Ser Phe Ile Arg Ile His Lys Val Met
305                 310                 315                 320
Lys Val Leu Asn Phe Thr Thr Lys Ala Lys Asp Leu His Leu Ser Asp
                325                 330                 335
Val Phe Leu Lys Ala Leu Asn His Leu Pro Leu Glu Tyr Asn Ser Ala
            340                 345                 350
Leu Tyr Ser Arg Ile Phe Asp Asp Phe Gly Thr His Tyr Phe Thr Ser
        355                 360                 365
Gly Ser Leu Gly Gly Val Tyr Asp Leu Leu Tyr Gln Phe Ser Ser Glu
    370                 375                 380
Glu Leu Lys Asn Ser Gly Leu Thr Glu Glu Glu Ala Lys His Cys Val
385                 390                 395                 400
Arg Ile Glu Thr Lys Lys Arg Val Leu Phe Ala Lys Lys Thr Lys Val
                405                 410                 415
Glu His Arg Cys Thr Thr Asn Lys Leu Ser Glu Lys His Glu Gly Ser
            420                 425                 430
Phe Ile Gln Gly Ala Glu Lys Ser Ile Ser Leu Ile Arg Gly Gly Arg
        435                 440                 445
Ser Glu Tyr Gly Ala Ala Leu Ala Trp Glu Lys Gly Ser Ser Gly Leu
    450                 455                 460
Glu Glu Lys Thr Phe Ser Glu Trp Leu Glu Ser Val Lys Glu Asn Pro
465                 470                 475                 480
Ala Val Ile Asp Phe Glu Leu Ala Pro Ile Val Asp Leu Val Arg Asn
                485                 490                 495
Ile Pro Cys Ala Val Thr Lys Arg Asn Asn Leu Arg Lys Ala Leu Gln
            500                 505                 510
Glu Tyr Ala Ala Lys Phe Asp Pro Cys Gln Cys Ala Pro Cys Pro Asn
        515                 520                 525
Asn Gly Arg Pro Thr Leu Ser Gly Thr Glu Cys Leu Cys Val Cys Gln
    530                 535                 540
Ser Gly Thr Tyr Gly Glu Asn Cys Glu Lys Gln Ser Pro Asp Tyr Lys
545                 550                 555                 560
Ser Asn Ala Val Asp Gly Gln Trp Gly Cys Trp Ser Ser Trp Ser Thr
                565                 570                 575
Cys Asp Ala Thr Tyr Lys Arg Ser Arg Thr Arg Glu Cys Asn Asn Pro
            580                 585                 590
Ala Pro Gln Arg Gly Gly Lys Arg Cys Glu Gly Glu Lys Arg Gln Glu
        595                 600                 605
Glu Asp Cys Thr Phe Ser Ile Met Glu Asn Asn Gly Gln Pro Cys Ile
```

```
    610                 615                 620
Asn Asp Asp Glu Glu Met Lys Glu Val Asp Leu Pro Glu Ile Glu Ala
625                 630                 635                 640
Asp Ser Gly Cys Pro Gln Pro Val Pro Pro Glu Asn Gly Phe Ile Arg
                645                 650                 655
Asn Glu Lys Gln Leu Tyr Leu Val Gly Glu Asp Val Glu Ile Ser Cys
            660                 665                 670
Leu Thr Gly Phe Glu Thr Val Gly Tyr Gln Tyr Phe Arg Cys Leu Pro
        675                 680                 685
Asp Gly Thr Trp Arg Gln Gly Asp Val Glu Cys Gln Arg Thr Glu Cys
    690                 695                 700
Ile Lys Pro Val Val Gln Glu Val Leu Thr Ile Thr Pro Phe Gln Arg
705                 710                 715                 720
Leu Tyr Arg Ile Gly Glu Ser Ile Glu Leu Thr Cys Pro Lys Gly Phe
                725                 730                 735
Val Val Ala Gly Pro Ser Arg Tyr Thr Cys Gln Gly Asn Ser Trp Thr
            740                 745                 750
Pro Pro Ile Ser Asn Ser Leu Thr Cys Glu Lys Asp Thr Leu Thr Lys
        755                 760                 765
Leu Lys Gly His Cys Gln Leu Gly Gln Lys Gln Ser Gly Ser Glu Cys
    770                 775                 780
Ile Cys Met Ser Pro Glu Glu Asp Cys Ser His His Ser Glu Asp Leu
785                 790                 795                 800
Cys Val Phe Asp Thr Asp Ser Asn Asp Tyr Phe Thr Ser Pro Ala Cys
                805                 810                 815
Lys Phe Leu Ala Glu Lys Cys Leu Asn Asn Gln Gln Leu His Phe Leu
            820                 825                 830
His Ile Gly Ser Cys Gln Asp Gly Arg Gln Leu Glu Trp Gly Leu Glu
        835                 840                 845
Arg Thr Arg Leu Ser Ser Asn Ser Thr Lys Lys Glu Ser Cys Gly Tyr
    850                 855                 860
Asp Thr Cys Tyr Asp Trp Glu Lys Cys Ser Ala Ser Thr Ser Lys Cys
865                 870                 875                 880
Val Cys Leu Leu Pro Pro Gln Cys Phe Lys Gly Gly Asn Gln Leu Tyr
                885                 890                 895
Cys Val Lys Met Gly Ser Ser Thr Ser Glu Lys Thr Leu Asn Ile Cys
            900                 905                 910
Glu Val Gly Thr Ile Arg Cys Ala Asn Arg Lys Met Glu Ile Leu His
        915                 920                 925
Pro Gly Lys Cys Leu Ala
    930
```

<210> 316
<211> 843
<212> PRT
<213> Homo sapiens

<400> 316

```
Met Lys Val Ile Ser Leu Phe Ile Leu Val Gly Phe Ile Gly Glu Phe
 1               5                  10                  15
Gln Ser Phe Ser Ser Ala Ser Ser Pro Val Asn Cys Gln Trp Asp Phe
            20                  25                  30
Tyr Ala Pro Trp Ser Glu Cys Asn Gly Cys Thr Lys Thr Gln Thr Arg
        35                  40                  45
Arg Arg Ser Val Ala Val Tyr Gly Gln Tyr Gly Gly Gln Pro Cys Val
    50                  55                  60
Gly Asn Ala Phe Glu Thr Gln Ser Cys Glu Pro Thr Arg Gly Cys Pro
```

65 70 75 80
Thr Glu Glu Gly Cys Gly Glu Arg Phe Arg Cys Phe Ser Gly Gln Cys
85 90 95
Ile Ser Lys Ser Leu Val Cys Asn Gly Asp Ser Asp Cys Asp Glu Asp
100 105 110
Ser Ala Asp Glu Asp Arg Cys Glu Asp Ser Glu Arg Arg Pro Ser Cys
115 120 125
Asp Ile Asp Lys Pro Pro Pro Asn Ile Glu Leu Thr Gly Asn Gly Tyr
130 135 140
Asn Glu Leu Thr Gly Gln Phe Arg Asn Arg Val Ile Asn Thr Lys Ser
145 150 155 160
Phe Gly Gly Gln Cys Arg Lys Val Phe Ser Gly Asp Gly Lys Asp Phe
165 170 175
Tyr Arg Leu Ser Gly Asn Val Leu Ser Tyr Thr Phe Gln Val Lys Ile
180 185 190
Asn Asn Asp Phe Asn Tyr Glu Phe Tyr Asn Ser Thr Trp Ser Tyr Val
195 200 205
Lys His Thr Ser Thr Glu His Thr Ser Ser Ser Arg Lys Arg Ser Phe
210 215 220
Phe Arg Ser Ser Ser Ser Ser Ser Ser Arg Ser Tyr Thr Ser His Thr Asn
225 230 235 240
Glu Ile His Lys Gly Lys Ser Tyr Gln Leu Leu Val Val Glu Asn Thr
245 250 255
Val Glu Val Ala Gln Phe Ile Asn Asn Asn Pro Glu Phe Leu Gln Leu
260 265 270
Ala Glu Pro Phe Trp Lys Glu Leu Ser His Leu Pro Ser Leu Tyr Asp
275 280 285
Tyr Ser Ala Tyr Arg Arg Leu Ile Asp Gln Tyr Gly Thr His Tyr Leu
290 295 300
Gln Ser Gly Ser Leu Gly Gly Glu Tyr Arg Val Leu Phe Tyr Val Asp
305 310 315 320
Ser Glu Lys Leu Lys Gln Asn Asp Phe Asn Ser Val Glu Glu Lys Lys
325 330 335
Cys Lys Ser Ser Gly Trp His Phe Val Val Lys Phe Ser Ser His Gly
340 345 350
Cys Lys Glu Leu Glu Asn Ala Leu Lys Ala Ala Ser Gly Thr Gln Asn
355 360 365
Asn Val Leu Arg Gly Glu Pro Phe Ile Arg Gly Gly Gly Ala Gly Phe
370 375 380
Ile Ser Gly Leu Ser Tyr Leu Glu Leu Asp Asn Pro Ala Gly Asn Lys
385 390 395 400
Arg Arg Tyr Ser Ala Trp Ala Glu Ser Val Thr Asn Leu Pro Gln Val
405 410 415
Ile Lys Gln Lys Leu Thr Pro Leu Tyr Glu Leu Val Lys Glu Val Pro
420 425 430
Cys Ala Ser Val Lys Lys Leu Tyr Leu Lys Trp Ala Leu Glu Glu Tyr
435 440 445
Leu Asp Glu Phe Asp Pro Cys His Cys Arg Pro Cys Gln Asn Gly Gly
450 455 460
Leu Ala Thr Val Glu Gly Thr His Cys Leu Cys His Cys Lys Pro Tyr
465 470 475 480
Thr Phe Gly Ala Ala Cys Glu Gln Gly Val Leu Val Gly Asn Gln Ala
485 490 495
Gly Gly Val Asp Gly Gly Trp Ser Cys Trp Ser Ser Trp Ser Pro Cys
500 505 510
Val Gln Gly Lys Lys Thr Arg Ser Arg Glu Cys Asn Asn Pro Pro Pro
515 520 525
Ser Gly Gly Gly Arg Ser Cys Val Gly Glu Thr Thr Glu Ser Thr Gln

```
    530                 535                 540
Cys Glu Asp Glu Glu Leu Glu His Leu Arg Leu Leu Glu Pro His Cys
545                 550                 555                 560
Phe Pro Leu Ser Leu Val Pro Thr Glu Phe Cys Pro Ser Pro Pro Ala
                565                 570                 575
Leu Lys Asp Gly Phe Val Gln Asp Glu Gly Thr Met Phe Pro Val Gly
            580                 585                 590
Lys Asn Val Val Tyr Thr Cys Asn Glu Gly Tyr Ser Leu Ile Gly Asn
        595                 600                 605
Pro Val Ala Arg Cys Gly Glu Asp Leu Arg Trp Leu Val Gly Glu Met
    610                 615                 620
His Cys Gln Lys Ile Ala Cys Val Leu Pro Val Leu Met Asp Gly Ile
625                 630                 635                 640
Gln Ser His Pro Gln Lys Pro Phe Tyr Thr Val Gly Glu Lys Val Thr
                645                 650                 655
Val Ser Cys Ser Gly Gly Met Ser Leu Glu Gly Pro Ser Ala Phe Leu
            660                 665                 670
Cys Gly Ser Ser Leu Lys Trp Ser Pro Glu Met Lys Asn Ala Arg Cys
        675                 680                 685
Val Gln Lys Glu Asn Pro Leu Thr Gln Ala Val Pro Lys Cys Gln Arg
    690                 695                 700
Trp Glu Lys Leu Gln Asn Ser Arg Cys Val Cys Lys Met Pro Tyr Glu
705                 710                 715                 720
Cys Gly Pro Ser Leu Asp Val Cys Ala Gln Asp Glu Arg Ser Lys Arg
                725                 730                 735
Ile Leu Pro Leu Thr Val Cys Lys Met His Val Leu His Cys Gln Gly
            740                 745                 750
Arg Asn Tyr Thr Leu Thr Gly Arg Asp Ser Cys Thr Leu Pro Ala Ser
        755                 760                 765
Ala Glu Lys Ala Cys Gly Ala Cys Pro Leu Trp Gly Lys Cys Asp Ala
    770                 775                 780
Glu Ser Ser Lys Cys Val Cys Arg Glu Ala Ser Glu Cys Glu Glu Glu
785                 790                 795                 800
Gly Phe Ser Ile Cys Val Glu Val Asn Gly Lys Glu Gln Thr Met Ser
                805                 810                 815
Glu Cys Glu Ala Gly Ala Leu Arg Cys Arg Gly Gln Ser Ile Ser Val
            820                 825                 830
Thr Ser Ile Arg Pro Cys Ala Ala Glu Thr Gln
        835                 840
```

<210> 317
<211> 584
<212> PRT
<213> Homo sapiens

<400> 317

```
Met Phe Ala Val Val Phe Phe Ile Leu Ser Leu Met Thr Cys Gln Pro
 1                5                  10                  15
Gly Val Thr Ala Gln Glu Lys Val Asn Gln Arg Val Arg Arg Ala Ala
            20                  25                  30
Thr Pro Ala Ala Val Thr Cys Gln Leu Ser Asn Trp Ser Glu Trp Thr
        35                  40                  45
Asp Cys Phe Pro Cys Gln Asp Lys Lys Tyr Arg His Arg Ser Leu Leu
    50                  55                  60
Gln Pro Asn Lys Phe Gly Gly Thr Ile Cys Ser Gly Asp Ile Trp Asp
65                  70                  75                  80
Gln Ala Ser Cys Ser Ser Ser Thr Thr Cys Val Arg Gln Ala Gln Cys
```

```
                85                  90                  95
Gly Gln Asp Phe Gln Cys Lys Glu Thr Gly Arg Cys Leu Lys Arg His
            100                 105                 110
Leu Val Cys Asn Gly Asp Gln Asp Cys Leu Asp Gly Ser Asp Glu Asp
        115                 120                 125
Asp Cys Glu Asp Val Arg Ala Ile Asp Glu Asp Cys Ser Gln Tyr Glu
    130                 135                 140
Pro Ile Pro Gly Ser Gln Lys Ala Ala Leu Gly Tyr Asn Ile Leu Thr
145                 150                 155                 160
Gln Glu Asp Ala Gln Ser Val Tyr Asp Ala Ser Tyr Tyr Gly Gly Gln
                165                 170                 175
Cys Glu Thr Val Tyr Asn Gly Glu Trp Arg Glu Leu Arg Tyr Asp Ser
            180                 185                 190
Thr Cys Glu Arg Leu Tyr Tyr Gly Asp Asp Glu Lys Tyr Phe Arg Lys
        195                 200                 205
Pro Tyr Asn Phe Leu Lys Tyr His Phe Glu Ala Leu Ala Asp Thr Gly
    210                 215                 220
Ile Ser Ser Glu Phe Tyr Asp Asn Ala Asn Asp Leu Leu Ser Lys Val
225                 230                 235                 240
Lys Lys Asp Lys Ser Asp Ser Phe Gly Val Thr Ile Gly Ile Gly Pro
                245                 250                 255
Ala Gly Ser Pro Leu Leu Val Gly Val Gly Val Ser His Ser Gln Asp
            260                 265                 270
Thr Ser Phe Leu Asn Glu Leu Asn Lys Tyr Asn Glu Lys Lys Phe Ile
        275                 280                 285
Phe Thr Arg Ile Phe Thr Lys Val Gln Thr Ala His Phe Lys Met Arg
    290                 295                 300
Lys Asp Asp Ile Met Leu Asp Glu Gly Met Leu Gln Ser Leu Met Glu
305                 310                 315                 320
Leu Pro Asp Gln Tyr Asn Tyr Gly Met Tyr Ala Lys Phe Ile Asn Asp
                325                 330                 335
Tyr Gly Thr His Tyr Ile Thr Ser Gly Ser Met Gly Gly Ile Tyr Glu
            340                 345                 350
Tyr Ile Leu Val Ile Asp Lys Ala Lys Met Glu Ser Leu Gly Ile Thr
        355                 360                 365
Ser Arg Asp Ile Thr Thr Cys Phe Gly Gly Ser Leu Gly Ile Gln Tyr
    370                 375                 380
Glu Asp Lys Ile Asn Val Gly Gly Gly Leu Ser Gly Asp His Cys Lys
385                 390                 395                 400
Lys Phe Gly Gly Gly Lys Thr Glu Arg Ala Arg Lys Ala Met Ala Val
                405                 410                 415
Glu Asp Ile Ile Ser Arg Val Arg Gly Gly Ser Ser Gly Trp Ser Gly
            420                 425                 430
Gly Leu Ala Gln Asn Arg Ser Thr Ile Thr Tyr Arg Ser Trp Gly Arg
        435                 440                 445
Ser Leu Lys Tyr Asn Pro Val Val Ile Asp Phe Glu Met Gln Pro Ile
    450                 455                 460
His Glu Val Leu Arg His Thr Ser Leu Gly Pro Leu Glu Ala Lys Arg
465                 470                 475                 480
Gln Asn Leu Arg Arg Ala Leu Asp Gln Tyr Leu Met Glu Phe Asn Ala
                485                 490                 495
Cys Arg Cys Gly Pro Cys Phe Asn Asn Gly Val Pro Ile Leu Glu Gly
            500                 505                 510
Thr Ser Cys Arg Cys Gln Cys Arg Leu Gly Ser Leu Gly Ala Ala Cys
        515                 520                 525
Glu Gln Thr Gln Thr Glu Gly Ala Lys Ala Asp Gly Ser Trp Ser Cys
    530                 535                 540
Trp Ser Ser Trp Ser Val Cys Arg Ala Gly Ile Gln Glu Arg Arg Arg
```

545 550 555 560
Glu Cys Asp Asn Pro Ala Pro Gln Asn Gly Gly Ala Ser Cys Pro Gly
565 570 575
Arg Lys Val Gln Thr Gln Ala Cys
580

<210> 318
<211> 591
<212> PRT
<213> Homo sapiens

<400> 318
Met Lys Asn Ser Arg Thr Trp Ala Trp Arg Ala Pro Val Glu Leu Phe
1 5 10 15
Leu Leu Cys Ala Ala Leu Gly Cys Leu Ser Leu Pro Gly Ser Arg Gly
20 25 30
Glu Arg Pro His Ser Phe Gly Ser Asn Ala Val Asn Lys Ser Phe Ala
35 40 45
Lys Ser Arg Gln Met Arg Ser Val Asp Val Thr Leu Met Pro Ile Asp
50 55 60
Cys Glu Leu Ser Ser Trp Ser Ser Trp Thr Thr Cys Asp Pro Cys Gln
65 70 75 80
Lys Lys Arg Tyr Arg Tyr Ala Tyr Leu Leu Gln Pro Ser Gln Phe His
85 90 95
Gly Glu Pro Cys Asn Phe Ser Asp Lys Glu Val Glu Asp Cys Val Thr
100 105 110
Asn Arg Pro Cys Arg Ser Gln Val Arg Cys Glu Gly Phe Val Cys Ala
115 120 125
Gln Thr Gly Arg Cys Val Asn Arg Arg Leu Leu Cys Asn Gly Asp Asn
130 135 140
Asp Cys Gly Asp Gln Ser Asp Glu Ala Asn Cys Arg Arg Ile Tyr Lys
145 150 155 160
Lys Cys Gln His Glu Met Asp Gln Tyr Trp Gly Ile Gly Ser Leu Ala
165 170 175
Ser Gly Ile Asn Leu Phe Thr Asn Ser Phe Glu Gly Pro Val Leu Asp
180 185 190
His Arg Tyr Tyr Ala Gly Gly Cys Ser Pro His Tyr Ile Leu Asn Thr
195 200 205
Arg Phe Arg Lys Pro Tyr Asn Val Glu Ser Tyr Thr Pro Gln Thr Gln
210 215 220
Gly Lys Tyr Glu Phe Ile Leu Lys Glu Tyr Glu Ser Tyr Ser Asp Phe
225 230 235 240
Glu Arg Asn Val Thr Glu Lys Met Ala Ser Lys Ser Gly Phe Ser Phe
245 250 255
Gly Phe Lys Ile Pro Gly Ile Phe Glu Leu Gly Ile Ser Ser Gln Ser
260 265 270
Asp Arg Gly Lys His Tyr Ile Arg Arg Thr Lys Arg Phe Ser His Thr
275 280 285
Lys Ser Val Phe Leu His Ala Arg Ser Asp Leu Glu Val Ala His Tyr
290 295 300
Lys Leu Lys Pro Arg Ser Leu Met Leu His Tyr Glu Phe Leu Gln Arg
305 310 315 320
Val Lys Arg Leu Pro Leu Glu Tyr Ser Tyr Gly Glu Tyr Arg Asp Leu
325 330 335
Phe Arg Asp Phe Gly Thr His Tyr Ile Thr Glu Ala Val Leu Gly Gly
340 345 350
Ile Tyr Glu Tyr Thr Leu Val Met Asn Lys Glu Ala Met Glu Arg Gly

```
        355                 360                 365
Asp Tyr Thr Leu Asn Asn Val His Ala Cys Ala Lys Asn Asp Phe Lys
    370                 375                 380
Ile Gly Gly Ala Ile Glu Glu Val Tyr Val Ser Leu Gly Val Ser Val
385                 390                 395                 400
Gly Lys Cys Arg Gly Ile Leu Asn Glu Ile Lys Asp Arg Asn Lys Arg
                405                 410                 415
Asp Thr Met Val Glu Asp Leu Val Val Leu Val Arg Gly Gly Ala Ser
            420                 425                 430
Glu His Ile Thr Thr Leu Ala Tyr Gln Glu Leu Pro Thr Ala Asp Leu
        435                 440                 445
Met Gln Glu Trp Gly Asp Ala Val Gln Tyr Asn Pro Ala Ile Ile Lys
    450                 455                 460
Val Lys Val Glu Pro Leu Tyr Glu Leu Val Thr Ala Thr Asp Phe Ala
465                 470                 475                 480
Tyr Ser Ser Thr Val Arg Gln Asn Met Lys Gln Ala Leu Glu Glu Phe
                485                 490                 495
Gln Lys Glu Val Ser Ser Cys His Cys Ala Pro Cys Gln Gly Asn Gly
            500                 505                 510
Val Pro Val Leu Lys Gly Ser Arg Cys Asp Cys Ile Cys Pro Val Gly
        515                 520                 525
Ser Gln Gly Leu Ala Cys Glu Val Ser Tyr Arg Lys Asn Thr Pro Ile
    530                 535                 540
Asp Gly Lys Trp Asn Cys Trp Ser Asn Trp Ser Ser Cys Ser Gly Arg
545                 550                 555                 560
Arg Lys Thr Arg Gln Arg Gln Cys Asn Asn Pro Pro Pro Gln Asn Gly
                565                 570                 575
Gly Ser Pro Cys Ser Gly Pro Ala Ser Glu Thr Leu Asp Cys Ser
            580                 585                 590
```

<210> 319
<211> 202
<212> PRT
<213> Homo sapiens

<400> 319

```
Met Leu Pro Pro Gly Thr Ala Thr Leu Leu Thr Leu Leu Leu Ala Ala
 1               5                  10                  15
Gly Ser Leu Gly Gln Lys Pro Gln Arg Pro Arg Arg Pro Ala Ser Pro
            20                  25                  30
Ile Ser Thr Ile Gln Pro Lys Ala Asn Phe Asp Ala Gln Gln Phe Ala
        35                  40                  45
Gly Thr Trp Leu Leu Val Ala Val Gly Ser Ala Cys Arg Phe Leu Gln
    50                  55                  60
Glu Gln Gly His Arg Ala Glu Ala Thr Thr Leu His Val Ala Pro Gln
65                  70                  75                  80
Gly Thr Ala Met Ala Val Ser Thr Phe Arg Lys Leu Asp Gly Ile Cys
                85                  90                  95
Trp Gln Val Arg Gln Leu Tyr Gly Asp Thr Gly Val Leu Gly Arg Phe
            100                 105                 110
Leu Leu Gln Ala Arg Gly Ala Arg Gly Ala Val His Val Val Val Ala
        115                 120                 125
Glu Thr Asp Tyr Gln Ser Phe Ala Val Leu Tyr Leu Glu Arg Ala Gly
    130                 135                 140
Gln Leu Ser Val Lys Leu Tyr Ala Arg Ser Leu Pro Val Ser Asp Ser
145                 150                 155                 160
Val Leu Ser Gly Phe Glu Gln Arg Val Gln Glu Ala His Leu Thr Glu
```

```
                165                 170                 175
Asp Gln Ile Phe Tyr Phe Pro Lys Tyr Gly Phe Cys Glu Ala Ala Asp
            180                 185                 190
Gln Phe His Val Leu Asp Glu Val Arg Arg
        195                 200
```

<210> 320
<211> 559
<212> PRT
<213> Homo sapiens

<400> 320

```
Met Ser Ala Cys Arg Ser Phe Ala Val Ala Ile Cys Ile Leu Glu Ile
 1               5                  10                  15
Ser Ile Leu Thr Ala Gln Tyr Thr Thr Ser Tyr Asp Pro Glu Leu Thr
            20                  25                  30
Glu Ser Ser Gly Ser Ala Ser His Ile Asp Cys Arg Met Ser Pro Trp
        35                  40                  45
Ser Glu Trp Ser Gln Cys Asp Pro Cys Leu Arg Gln Met Phe Arg Ser
    50                  55                  60
Arg Ser Ile Glu Val Phe Gly Gln Phe Asn Gly Lys Arg Cys Thr Asp
65                  70                  75                  80
Ala Val Gly Asp Arg Arg Gln Cys Val Pro Thr Glu Pro Cys Glu Asp
                85                  90                  95
Ala Glu Asp Asp Cys Gly Asn Asp Phe Gln Cys Ser Thr Gly Arg Cys
            100                 105                 110
Ile Lys Met Arg Leu Arg Cys Asn Gly Asp Asn Asp Cys Gly Asp Phe
        115                 120                 125
Ser Asp Glu Asp Asp Cys Glu Ser Glu Pro Arg Pro Pro Cys Arg Asp
    130                 135                 140
Arg Val Val Glu Glu Ser Glu Leu Ala Arg Thr Ala Gly Tyr Gly Ile
145                 150                 155                 160
Asn Ile Leu Gly Met Asp Pro Leu Ser Thr Pro Phe Asp Asn Glu Phe
                165                 170                 175
Tyr Asn Gly Leu Cys Asn Arg Asp Arg Asp Gly Asn Thr Leu Thr Tyr
            180                 185                 190
Tyr Arg Arg Pro Trp Asn Val Ala Ser Leu Ile Tyr Glu Thr Lys Gly
        195                 200                 205
Glu Lys Asn Phe Arg Thr Glu His Tyr Glu Glu Gln Ile Glu Ala Phe
    210                 215                 220
Lys Ser Ile Ile Gln Glu Lys Thr Ser Asn Phe Asn Ala Ala Ile Ser
225                 230                 235                 240
Leu Lys Phe Thr Pro Thr Glu Thr Asn Lys Ala Glu Gln Cys Cys Glu
                245                 250                 255
Glu Thr Ala Ser Ser Ile Ser Leu His Gly Lys Gly Ser Phe Arg Phe
            260                 265                 270
Ser Tyr Ser Lys Asn Glu Thr Tyr Gln Leu Phe Leu Ser Tyr Ser Ser
        275                 280                 285
Lys Lys Glu Lys Met Phe Leu His Val Lys Gly Glu Ile His Leu Gly
    290                 295                 300
Arg Phe Val Met Arg Asn Arg Asp Val Val Leu Thr Thr Thr Phe Val
305                 310                 315                 320
Asp Asp Ile Lys Ala Leu Pro Thr Thr Tyr Glu Lys Gly Glu Tyr Phe
                325                 330                 335
Ala Phe Leu Glu Thr Tyr Gly Thr His Tyr Ser Ser Ser Gly Ser Leu
            340                 345                 350
Gly Gly Leu Tyr Glu Leu Ile Tyr Val Leu Asp Lys Ala Ser Met Lys
```

```
        355                 360                 365
Arg Lys Gly Val Glu Leu Lys Asp Ile Lys Arg Cys Leu Gly Tyr His
    370                 375                 380
Leu Asp Val Ser Leu Ala Phe Ser Glu Ile Ser Val Gly Ala Glu Phe
385                 390                 395                 400
Asn Lys Asp Asp Cys Val Lys Arg Gly Glu Gly Arg Ala Val Asn Ile
                405                 410                 415
Thr Ser Glu Asn Leu Ile Asp Asp Val Val Ser Leu Ile Arg Gly Gly
            420                 425                 430
Thr Arg Lys Tyr Ala Phe Glu Leu Lys Glu Lys Leu Leu Arg Gly Thr
        435                 440                 445
Val Ile Asp Val Thr Asp Phe Val Asn Trp Ala Ser Ser Ile Asn Asp
    450                 455                 460
Ala Pro Val Leu Ile Ser Gln Lys Leu Ser Pro Ile Tyr Asn Leu Val
465                 470                 475                 480
Pro Val Lys Met Lys Asn Ala His Leu Lys Lys Gln Asn Leu Glu Arg
                485                 490                 495
Ala Ile Glu Asp Tyr Ile Asn Glu Phe Ser Val Arg Lys Cys His Thr
            500                 505                 510
Cys Gln Asn Gly Gly Thr Val Ile Leu Met Asp Gly Lys Cys Leu Cys
        515                 520                 525
Ala Cys Pro Phe Lys Phe Glu Gly Ile Ala Cys Glu Ile Ser Lys Gln
    530                 535                 540
Lys Ile Ser Glu Gly Leu Pro Ala Leu Glu Phe Pro Asn Glu Lys
545                 550                 555
```

<210> 321
<211> 2039
<212> PRT
<213> Homo sapiens

<400> 321

```
Met Gly Ala Ser Ser Pro Arg Ser Pro Glu Pro Val Gly Pro Pro Ala
 1               5                  10                  15
Pro Gly Leu Pro Phe Cys Cys Gly Gly Ser Leu Leu Ala Val Val Val
            20                  25                  30
Leu Leu Ala Leu Pro Val Ala Trp Gly Gln Cys Asn Ala Pro Glu Trp
        35                  40                  45
Leu Pro Phe Ala Arg Pro Thr Asn Leu Thr Asp Glu Phe Glu Phe Pro
    50                  55                  60
Ile Gly Thr Tyr Leu Asn Tyr Glu Cys Arg Pro Gly Tyr Ser Gly Arg
65                  70                  75                  80
Pro Phe Ser Ile Ile Cys Leu Lys Asn Ser Val Trp Thr Gly Ala Lys
                85                  90                  95
Asp Arg Cys Arg Arg Lys Ser Cys Arg Asn Pro Pro Asp Pro Val Asn
            100                 105                 110
Gly Met Val His Val Ile Lys Gly Ile Gln Phe Gly Ser Gln Ile Lys
        115                 120                 125
Tyr Ser Cys Thr Lys Gly Tyr Arg Leu Ile Gly Ser Ser Ser Ala Thr
    130                 135                 140
Cys Ile Ile Ser Gly Asp Thr Val Ile Trp Asp Asn Glu Thr Pro Ile
145                 150                 155                 160
Cys Asp Arg Ile Pro Cys Gly Leu Pro Pro Thr Ile Thr Asn Gly Asp
                165                 170                 175
Phe Ile Ser Thr Asn Arg Glu Asn Phe His Tyr Gly Ser Val Val Thr
            180                 185                 190
Tyr Arg Cys Asn Pro Gly Ser Gly Gly Arg Lys Val Phe Glu Leu Val
```

```
         195                 200                 205
Gly Glu Pro Ser Ile Tyr Cys Thr Ser Asn Asp Asp Gln Val Gly Ile
    210                 215                 220
Trp Ser Gly Pro Ala Pro Gln Cys Ile Ile Pro Asn Lys Cys Thr Pro
225                 230                 235                 240
Pro Asn Val Glu Asn Gly Ile Leu Val Ser Asp Asn Arg Ser Leu Phe
                245                 250                 255
Ser Leu Asn Glu Val Val Glu Phe Arg Cys Gln Pro Gly Phe Val Met
            260                 265                 270
Lys Gly Pro Arg Arg Val Lys Cys Gln Ala Leu Asn Lys Trp Glu Pro
        275                 280                 285
Glu Leu Pro Ser Cys Ser Arg Val Cys Gln Pro Pro Pro Asp Val Leu
    290                 295                 300
His Ala Glu Arg Thr Gln Arg Asp Lys Asp Asn Phe Ser Pro Gly Gln
305                 310                 315                 320
Glu Val Phe Tyr Ser Cys Glu Pro Gly Tyr Asp Leu Arg Gly Ala Ala
                325                 330                 335
Ser Met Arg Cys Thr Pro Gln Gly Asp Trp Ser Pro Ala Ala Pro Thr
            340                 345                 350
Cys Glu Val Lys Ser Cys Asp Asp Phe Met Gly Gln Leu Leu Asn Gly
        355                 360                 365
Arg Val Leu Phe Pro Val Asn Leu Gln Leu Gly Ala Lys Val Asp Phe
    370                 375                 380
Val Cys Asp Glu Gly Phe Gln Leu Lys Gly Ser Ser Ala Ser Tyr Cys
385                 390                 395                 400
Val Leu Ala Gly Met Glu Ser Leu Trp Asn Ser Ser Val Pro Val Cys
                405                 410                 415
Glu Gln Ile Phe Cys Pro Ser Pro Pro Val Ile Pro Asn Gly Arg His
            420                 425                 430
Thr Gly Lys Pro Leu Glu Val Phe Pro Phe Gly Lys Ala Val Asn Tyr
        435                 440                 445
Thr Cys Asp Pro His Pro Asp Arg Gly Thr Ser Phe Asp Leu Ile Gly
    450                 455                 460
Glu Ser Thr Ile Arg Cys Thr Ser Asp Pro Gln Gly Asn Gly Val Trp
465                 470                 475                 480
Ser Ser Pro Ala Pro Arg Cys Gly Ile Leu Gly His Cys Gln Ala Pro
                485                 490                 495
Asp His Phe Leu Phe Ala Lys Leu Lys Thr Gln Thr Asn Ala Ser Asp
            500                 505                 510
Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu Cys Arg Pro Glu Tyr Tyr
        515                 520                 525
Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp Asn Leu Val Trp Ser Ser
    530                 535                 540
Pro Lys Asp Val Cys Lys Arg Lys Ser Cys Lys Thr Pro Pro Asp Pro
545                 550                 555                 560
Val Asn Gly Met Val His Val Ile Thr Asp Ile Gln Val Gly Ser Arg
                565                 570                 575
Ile Asn Tyr Ser Cys Thr Thr Gly His Arg Leu Ile Gly His Ser Ser
            580                 585                 590
Ala Glu Cys Ile Leu Ser Gly Asn Ala Ala His Trp Ser Thr Lys Pro
        595                 600                 605
Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu Pro Pro Thr Ile Ala Asn
    610                 615                 620
Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn Phe His Tyr Gly Ser Val
625                 630                 635                 640
Val Thr Tyr Arg Cys Asn Pro Gly Ser Gly Gly Arg Lys Val Phe Glu
                645                 650                 655
Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr Ser Asn Asp Asp Gln Val
```

```
                660                 665                 670
Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys Ile Ile Pro Asn Lys Cys
            675                 680                 685
Thr Pro Pro Asn Val Glu Asn Gly Ile Leu Val Ser Asp Asn Arg Ser
    690                 695                 700
Leu Phe Ser Leu Asn Glu Val Val Glu Phe Arg Cys Gln Pro Gly Phe
705                 710                 715                 720
Val Met Lys Gly Pro Arg Arg Val Lys Cys Gln Ala Leu Asn Lys Trp
                725                 730                 735
Glu Pro Glu Leu Pro Ser Cys Ser Arg Val Cys Gln Pro Pro Pro Asp
            740                 745                 750
Val Leu His Ala Glu Arg Thr Gln Arg Asp Lys Asp Asn Phe Ser Pro
        755                 760                 765
Gly Gln Glu Val Phe Tyr Ser Cys Glu Pro Gly Tyr Asp Leu Arg Gly
    770                 775                 780
Ala Ala Ser Met Arg Cys Thr Pro Gln Gly Asp Trp Ser Pro Ala Ala
785                 790                 795                 800
Pro Thr Cys Glu Val Lys Ser Cys Asp Asp Phe Met Gly Gln Leu Leu
                805                 810                 815
Asn Gly Arg Val Leu Phe Pro Val Asn Leu Gln Leu Gly Ala Lys Val
            820                 825                 830
Asp Phe Val Cys Asp Glu Gly Phe Gln Leu Lys Gly Ser Ser Ala Ser
        835                 840                 845
Tyr Cys Val Leu Ala Gly Met Glu Ser Leu Trp Asn Ser Ser Val Pro
    850                 855                 860
Val Cys Glu Gln Ile Phe Cys Pro Ser Pro Pro Val Ile Pro Asn Gly
865                 870                 875                 880
Arg His Thr Gly Lys Pro Leu Glu Val Phe Pro Phe Gly Lys Ala Val
                885                 890                 895
Asn Tyr Thr Cys Asp Pro His Pro Asp Arg Gly Thr Ser Phe Asp Leu
            900                 905                 910
Ile Gly Glu Ser Thr Ile Arg Cys Thr Ser Asp Pro Gln Gly Asn Gly
        915                 920                 925
Val Trp Ser Ser Pro Ala Pro Arg Cys Gly Ile Leu Gly His Cys Gln
    930                 935                 940
Ala Pro Asp His Phe Leu Phe Ala Lys Leu Lys Thr Gln Thr Asn Ala
945                 950                 955                 960
Ser Asp Phe Pro Ile Gly Thr Ser Leu Lys Tyr Glu Cys Arg Pro Glu
                965                 970                 975
Tyr Tyr Gly Arg Pro Phe Ser Ile Thr Cys Leu Asp Asn Leu Val Trp
            980                 985                 990
Ser Ser Pro Lys Asp Val Cys Lys Arg Lys Ser Cys Lys Thr Pro Pro
        995                 1000                1005
Asp Pro Val Asn Gly Met Val His Val Ile Thr Asp Ile Gln Val Gly
    1010                1015                1020
Ser Arg Ile Asn Tyr Ser Cys Thr Thr Gly His Arg Leu Ile Gly His
1025                1030                1035                1040
Ser Ser Ala Glu Cys Ile Leu Ser Gly Asn Thr Ala His Trp Ser Thr
                1045                1050                1055
Lys Pro Pro Ile Cys Gln Arg Ile Pro Cys Gly Leu Pro Pro Thr Ile
            1060                1065                1070
Ala Asn Gly Asp Phe Ile Ser Thr Asn Arg Glu Asn Phe His Tyr Gly
        1075                1080                1085
Ser Val Val Thr Tyr Arg Cys Asn Leu Gly Ser Arg Gly Arg Lys Val
    1090                1095                1100
Phe Glu Leu Val Gly Glu Pro Ser Ile Tyr Cys Thr Ser Asn Asp Asp
1105                1110                1115                1120
Gln Val Gly Ile Trp Ser Gly Pro Ala Pro Gln Cys Ile Ile Pro Asn
```

```
                1125                1130                1135
Lys Cys Thr Pro Pro Asn Val Glu Asn Gly Ile Leu Val Ser Asp Asn
            1140                1145                1150
Arg Ser Leu Phe Ser Leu Asn Glu Val Val Glu Phe Arg Cys Gln Pro
        1155                1160                1165
Gly Phe Val Met Lys Gly Pro Arg Arg Val Lys Cys Gln Ala Leu Asn
    1170                1175                1180
Lys Trp Glu Pro Glu Leu Pro Ser Cys Ser Arg Val Cys Gln Pro Pro
1185                1190                1195                1200
Pro Glu Ile Leu His Gly Glu His Thr Pro Ser His Gln Asp Asn Phe
                1205                1210                1215
Ser Pro Gly Gln Glu Val Phe Tyr Ser Cys Glu Pro Gly Tyr Asp Leu
            1220                1225                1230
Arg Gly Ala Ala Ser Leu His Cys Thr Pro Gln Gly Asp Trp Ser Pro
        1235                1240                1245
Glu Ala Pro Arg Cys Ala Val Lys Ser Cys Asp Asp Phe Leu Gly Gln
    1250                1255                1260
Leu Pro His Gly Arg Val Leu Phe Pro Leu Asn Leu Gln Leu Gly Ala
1265                1270                1275                1280
Lys Val Ser Phe Val Cys Asp Glu Gly Phe Arg Leu Lys Gly Ser Ser
                1285                1290                1295
Val Ser His Cys Val Leu Val Gly Met Arg Ser Leu Trp Asn Asn Ser
            1300                1305                1310
Val Pro Val Cys Glu His Ile Phe Cys Pro Asn Pro Pro Ala Ile Leu
        1315                1320                1325
Asn Gly Arg His Thr Gly Thr Pro Ser Gly Asp Ile Pro Tyr Gly Lys
    1330                1335                1340
Glu Ile Ser Tyr Thr Cys Asp Pro His Pro Asp Arg Gly Met Thr Phe
1345                1350                1355                1360
Asn Leu Ile Gly Glu Ser Thr Ile Arg Cys Thr Ser Asp Pro His Gly
                1365                1370                1375
Asn Gly Val Trp Ser Ser Pro Ala Pro Arg Cys Glu Leu Ser Val Arg
            1380                1385                1390
Ala Gly His Cys Lys Thr Pro Glu Gln Phe Pro Phe Ala Ser Pro Thr
        1395                1400                1405
Ile Pro Ile Asn Asp Phe Glu Phe Pro Val Gly Thr Ser Leu Asn Tyr
    1410                1415                1420
Glu Cys Arg Pro Gly Tyr Phe Gly Lys Met Phe Ser Ile Ser Cys Leu
1425                1430                1435                1440
Glu Asn Leu Val Trp Ser Ser Val Glu Asp Asn Cys Arg Arg Lys Ser
                1445                1450                1455
Cys Gly Pro Pro Pro Glu Pro Phe Asn Gly Met Val His Ile Asn Thr
            1460                1465                1470
Asp Thr Gln Phe Gly Ser Thr Val Asn Tyr Ser Cys Asn Glu Gly Phe
        1475                1480                1485
Arg Leu Ile Gly Ser Pro Ser Thr Thr Cys Leu Val Ser Gly Asn Asn
    1490                1495                1500
Val Thr Trp Asp Lys Lys Ala Pro Ile Cys Glu Ile Ile Ser Cys Glu
1505                1510                1515                1520
Pro Pro Pro Thr Ile Ser Asn Gly Asp Phe Tyr Ser Asn Asn Arg Thr
                1525                1530                1535
Ser Phe His Asn Gly Thr Val Val Thr Tyr Gln Cys His Thr Gly Pro
            1540                1545                1550
Asp Gly Glu Gln Leu Phe Glu Leu Val Gly Glu Arg Ser Ile Tyr Cys
        1555                1560                1565
Thr Ser Lys Asp Asp Gln Val Gly Val Trp Ser Ser Pro Pro Pro Arg
    1570                1575                1580
Cys Ile Ser Thr Asn Lys Cys Thr Ala Pro Glu Val Glu Asn Ala Ile
```

1585 1590 1595 1600
Arg Val Pro Gly Asn Arg Ser Phe Phe Ser Leu Thr Glu Ile Ile Arg
1605 1610 1615
Phe Arg Cys Gln Pro Gly Phe Val Met Val Gly Ser His Thr Val Gln
1620 1625 1630
Cys Gln Thr Asn Gly Arg Trp Gly Pro Lys Leu Pro His Cys Ser Arg
1635 1640 1645
Val Cys Gln Pro Pro Pro Glu Ile Leu His Gly Glu His Thr Leu Ser
1650 1655 1660
His Gln Asp Asn Phe Ser Pro Gly Gln Glu Val Phe Tyr Ser Cys Glu
1665 1670 1675 1680
Pro Ser Tyr Asp Leu Arg Gly Ala Ala Ser Leu His Cys Thr Pro Gln
1685 1690 1695
Gly Asp Trp Ser Pro Glu Ala Pro Arg Cys Thr Val Lys Ser Cys Asp
1700 1705 1710
Asp Phe Leu Gly Gln Leu Pro His Gly Arg Val Leu Leu Pro Leu Asn
1715 1720 1725
Leu Gln Leu Gly Ala Lys Val Ser Phe Val Cys Asp Glu Gly Phe Arg
1730 1735 1740
Leu Lys Gly Arg Ser Ala Ser His Cys Val Leu Ala Gly Met Lys Ala
1745 1750 1755 1760
Leu Trp Asn Ser Ser Val Pro Val Cys Glu Gln Ile Phe Cys Pro Asn
1765 1770 1775
Pro Pro Ala Ile Leu Asn Gly Arg His Thr Gly Thr Pro Phe Gly Asp
1780 1785 1790
Ile Pro Tyr Gly Lys Glu Ile Ser Tyr Ala Cys Asp Thr His Pro Asp
1795 1800 1805
Arg Gly Met Thr Phe Asn Leu Ile Gly Glu Ser Ser Ile Arg Cys Thr
1810 1815 1820
Ser Asp Pro Gln Gly Asn Gly Val Trp Ser Ser Pro Ala Pro Arg Cys
1825 1830 1835 1840
Glu Leu Ser Val Pro Ala Ala Cys Pro His Pro Pro Lys Ile Gln Asn
1845 1850 1855
Gly His Tyr Ile Gly Gly His Val Ser Leu Tyr Leu Pro Gly Met Thr
1860 1865 1870
Ile Ser Tyr Thr Cys Asp Pro Gly Tyr Leu Leu Val Gly Lys Gly Phe
1875 1880 1885
Ile Phe Cys Thr Asp Gln Gly Ile Trp Ser Gln Leu Asp His Tyr Cys
1890 1895 1900
Lys Glu Val Asn Cys Ser Phe Pro Leu Phe Met Asn Gly Ile Ser Lys
1905 1910 1915 1920
Glu Leu Glu Met Lys Lys Val Tyr His Tyr Gly Asp Tyr Val Thr Leu
1925 1930 1935
Lys Cys Glu Asp Gly Tyr Thr Leu Glu Gly Ser Pro Trp Ser Gln Cys
1940 1945 1950
Gln Ala Asp Asp Arg Trp Asp Pro Pro Leu Ala Lys Cys Thr Ser Arg
1955 1960 1965
Ala His Asp Ala Leu Ile Val Gly Thr Leu Ser Gly Thr Ile Phe Phe
1970 1975 1980
Ile Leu Leu Ile Ile Phe Leu Ser Trp Ile Ile Leu Lys His Arg Lys
1985 1990 1995 2000
Gly Asn Asn Ala His Glu Asn Pro Lys Glu Val Ala Ile His Leu His
2005 2010 2015
Ser Gln Gly Gly Ser Ser Val His Pro Arg Thr Leu Gln Thr Asn Glu
2020 2025 2030
Glu Asn Ser Arg Val Leu Pro
2035

<210> 322
<211> 1033
<212> PRT
<213> Homo sapiens

<400> 322
Met Gly Ala Ala Gly Leu Leu Gly Val Phe Leu Ala Leu Val Ala Pro
1 5 10 15
Gly Val Leu Gly Ile Ser Cys Gly Ser Pro Pro Pro Ile Leu Asn Gly
20 25 30
Arg Ile Ser Tyr Tyr Ser Thr Pro Ile Ala Val Gly Thr Val Ile Arg
35 40 45
Tyr Ser Cys Ser Gly Thr Phe Arg Leu Ile Gly Glu Lys Ser Leu Leu
50 55 60
Cys Ile Thr Lys Asp Lys Val Asp Gly Thr Trp Asp Lys Pro Ala Pro
65 70 75 80
Lys Cys Glu Tyr Phe Asn Lys Tyr Ser Ser Cys Pro Glu Pro Ile Val
85 90 95
Pro Gly Gly Tyr Lys Ile Arg Gly Ser Thr Pro Tyr Arg His Gly Asp
100 105 110
Ser Val Thr Phe Ala Cys Lys Thr Asn Phe Ser Met Asn Gly Asn Lys
115 120 125
Ser Val Trp Cys Gln Ala Asn Asn Met Trp Gly Pro Thr Arg Leu Pro
130 135 140
Thr Cys Val Ser Val Phe Pro Leu Glu Cys Pro Ala Leu Pro Met Ile
145 150 155 160
His Asn Gly His His Thr Ser Glu Asn Val Gly Ser Ile Ala Pro Gly
165 170 175
Leu Ser Val Thr Tyr Ser Cys Glu Ser Gly Tyr Leu Leu Val Gly Glu
180 185 190
Lys Ile Ile Asn Cys Leu Ser Ser Gly Lys Trp Ser Ala Val Pro Pro
195 200 205
Thr Cys Glu Glu Ala Arg Cys Lys Ser Leu Gly Arg Phe Pro Asn Gly
210 215 220
Lys Val Lys Glu Pro Pro Ile Leu Arg Val Gly Val Thr Ala Asn Phe
225 230 235 240
Phe Cys Asp Glu Gly Tyr Arg Leu Gln Gly Pro Pro Ser Ser Arg Cys
245 250 255
Val Ile Ala Gly Gln Gly Val Ala Trp Thr Lys Met Pro Val Cys Glu
260 265 270
Glu Ile Phe Cys Pro Ser Pro Pro Pro Ile Leu Asn Gly Arg His Ile
275 280 285
Gly Asn Ser Leu Ala Asn Val Ser Tyr Gly Ser Ile Val Thr Tyr Thr
290 295 300
Cys Asp Pro Asp Pro Glu Glu Gly Val Asn Phe Ile Leu Ile Gly Glu
305 310 315 320
Ser Thr Leu Arg Cys Thr Val Asp Ser Gln Lys Thr Gly Thr Trp Ser
325 330 335
Gly Pro Ala Pro Arg Cys Glu Leu Ser Thr Ser Ala Val Gln Cys Pro
340 345 350
His Pro Gln Ile Leu Arg Gly Arg Met Val Ser Gly Gln Lys Asp Arg
355 360 365
Tyr Thr Tyr Asn Asp Thr Val Ile Phe Ala Cys Met Phe Gly Phe Thr
370 375 380
Leu Lys Gly Ser Lys Gln Ile Arg Cys Asn Ala Gln Gly Thr Trp Glu
385 390 395 400
Pro Ser Ala Pro Val Cys Glu Lys Glu Cys Gln Ala Pro Pro Asn Ile

```
                405                 410                 415
Leu Asn Gly Gln Lys Glu Asp Arg His Met Val Arg Phe Asp Pro Gly
            420                 425                 430
Thr Ser Ile Lys Tyr Ser Cys Asn Pro Gly Tyr Val Leu Val Gly Glu
        435                 440                 445
Glu Ser Ile Gln Cys Thr Ser Glu Gly Val Trp Thr Pro Pro Val Pro
    450                 455                 460
Gln Cys Lys Val Ala Ala Cys Glu Ala Thr Gly Arg Gln Leu Leu Thr
465                 470                 475                 480
Lys Pro Gln His Gln Phe Val Arg Pro Asp Val Asn Ser Ser Cys Gly
                485                 490                 495
Glu Gly Tyr Lys Leu Ser Gly Ser Val Tyr Gln Glu Cys Gln Gly Thr
            500                 505                 510
Ile Pro Trp Phe Met Glu Ile Arg Leu Cys Lys Glu Ile Thr Cys Pro
        515                 520                 525
Pro Pro Pro Val Ile Tyr Asn Gly Ala His Thr Gly Ser Ser Leu Glu
    530                 535                 540
Asp Phe Pro Tyr Gly Thr Thr Val Thr Tyr Thr Cys Asn Pro Gly Pro
545                 550                 555                 560
Glu Arg Gly Val Glu Phe Ser Leu Ile Gly Glu Ser Thr Ile Arg Cys
                565                 570                 575
Thr Ser Asn Asp Gln Glu Arg Gly Thr Trp Ser Gly Pro Ala Pro Leu
            580                 585                 590
Cys Lys Leu Ser Leu Leu Ala Val Gln Cys Ser His Val His Ile Ala
        595                 600                 605
Asn Gly Tyr Lys Ile Ser Gly Lys Glu Ala Pro Tyr Phe Tyr Asn Asp
    610                 615                 620
Thr Val Thr Phe Lys Cys Tyr Ser Gly Phe Thr Leu Lys Gly Ser Ser
625                 630                 635                 640
Gln Ile Arg Cys Lys Ala Asp Asn Thr Trp Asp Pro Glu Ile Pro Val
                645                 650                 655
Cys Glu Lys Glu Thr Cys Gln His Val Arg Gln Ser Leu Gln Glu Leu
            660                 665                 670
Pro Ala Gly Ser Arg Val Glu Leu Val Asn Thr Ser Cys Gln Asp Gly
        675                 680                 685
Tyr Gln Leu Thr Gly His Ala Tyr Gln Met Cys Gln Asp Ala Glu Asn
    690                 695                 700
Gly Ile Trp Phe Lys Lys Ile Pro Leu Cys Lys Val Ile His Cys His
705                 710                 715                 720
Pro Pro Pro Val Ile Val Asn Gly Lys His Thr Gly Met Met Ala Glu
                725                 730                 735
Asn Phe Leu Tyr Gly Asn Glu Val Ser Tyr Glu Cys Asp Gln Gly Phe
            740                 745                 750
Tyr Leu Leu Gly Glu Lys Lys Leu Gln Cys Arg Ser Asp Ser Lys Gly
        755                 760                 765
His Gly Ser Trp Ser Gly Pro Ser Pro Gln Cys Leu Arg Ser Pro Pro
    770                 775                 780
Val Thr Arg Cys Pro Asn Pro Glu Val Lys His Gly Tyr Lys Leu Asn
785                 790                 795                 800
Lys Thr His Ser Ala Tyr Ser His Asn Asp Ile Val Tyr Val Asp Cys
                805                 810                 815
Asn Pro Gly Phe Ile Met Asn Gly Ser Arg Val Ile Arg Cys His Thr
            820                 825                 830
Asp Asn Thr Trp Val Pro Gly Val Pro Thr Cys Ile Lys Lys Ala Phe
        835                 840                 845
Ile Gly Cys Pro Pro Pro Pro Lys Thr Pro Asn Gly Asn His Thr Gly
    850                 855                 860
Gly Asn Ile Ala Arg Phe Ser Pro Gly Met Ser Ile Leu Tyr Ser Cys
```

865 870 875 880
Asp Gln Gly Tyr Leu Leu Val Gly Glu Ala Leu Leu Leu Cys Thr His
885 890 895
Glu Gly Thr Trp Ser Gln Pro Ala Pro His Cys Lys Glu Val Asn Cys
900 905 910
Ser Ser Pro Ala Asp Met Asp Gly Ile Gln Lys Gly Leu Glu Pro Arg
915 920 925
Lys Met Tyr Gln Tyr Gly Ala Val Val Thr Leu Glu Cys Glu Asp Gly
930 935 940
Tyr Met Leu Glu Gly Ser Pro Gln Ser Gln Cys Gln Ser Asp His Gln
945 950 955 960
Trp Asn Pro Pro Leu Ala Val Cys Arg Ser Arg Ser Leu Ala Pro Val
965 970 975
Leu Cys Gly Ile Ala Ala Gly Leu Ile Leu Leu Thr Phe Leu Ile Val
980 985 990
Ile Thr Leu Tyr Val Ile Ser Lys His Arg Glu Arg Asn Tyr Tyr Thr
995 1000 1005
Asp Thr Ser Gln Lys Glu Ala Phe His Leu Glu Ala Arg Glu Val Tyr
1010 1015 1020
Ser Val Asp Pro Tyr Asn Pro Ala Ser
1025 1030

<210> 323
<211> 381
<212> PRT
<213> Homo sapiens

<400> 323
Met Thr Val Ala Arg Pro Ser Val Pro Ala Ala Leu Pro Leu Leu Gly
1 5 10 15
Glu Leu Pro Arg Leu Leu Leu Leu Val Leu Leu Cys Leu Pro Ala Val
20 25 30
Trp Gly Asp Cys Gly Leu Pro Pro Asp Val Pro Asn Ala Gln Pro Ala
35 40 45
Leu Glu Gly Arg Thr Ser Phe Pro Glu Asp Thr Val Ile Thr Tyr Lys
50 55 60
Cys Glu Glu Ser Phe Val Lys Ile Pro Gly Glu Lys Asp Ser Val Ile
65 70 75 80
Cys Leu Lys Gly Ser Gln Trp Ser Asp Ile Glu Glu Phe Cys Asn Arg
85 90 95
Ser Cys Glu Val Pro Thr Arg Leu Asn Ser Ala Ser Leu Lys Gln Pro
100 105 110
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130 135 140
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145 150 155 160
Lys Ser Cys Pro Asn Pro Gly Glu Ile Arg Asn Gly Gln Ile Asp Val
165 170 175
Pro Gly Gly Ile Leu Phe Gly Ala Thr Ile Ser Phe Ser Cys Asn Thr
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Gly Tyr Lys Leu Phe Gly Ser Thr Ser Ser Phe Cys Leu Ile Ser Gly
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Ser Ser Val Gln Trp Ser Asp Pro Leu Pro Glu Cys Arg Glu Ile Tyr
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Cys Pro Ala Pro Pro Gln Ile Asp Asn Gly Ile Ile Gln Gly Glu Arg

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<210> 324
<211> 500
<212> PRT
<213> Homo sapiens

<400> 324
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Gln Pro Thr Ile Gln Pro Thr Gln Pro Thr Thr Gln Leu Pro Thr Asp
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Arg Thr Leu Tyr Ser Ser Ser Pro Arg Val Leu Ser Asn Asn Ser Asp

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Lys Val Pro Met Met Asn Ser Lys Lys Tyr Pro Val Ala His Phe Ile
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Leu Ser Leu Val Ile Leu Val Pro Gln Asn Leu Lys His Arg Leu Glu
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Asp Met Glu Gln Ala Leu Ser Pro Ser Val Phe Lys Ala Ile Met Glu
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Lys Leu Glu Met Ser Lys Phe Gln Pro Thr Leu Leu Thr Leu Pro Arg
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Glu Phe Phe Asp Phe Ser Tyr Asp Leu Asn Leu Cys Gly Leu Thr Glu
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<210> 325
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<212> DNA
<213> Homo sapiens

<400> 325

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<211> 699
<212> PRT
<213> Homo sapiens

<400> 326

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Ser Pro Gly Tyr Pro Asp Ser Tyr Pro Ser Asp Ser Glu Val Thr Trp
        35                  40                  45
Asn Ile Thr Val Pro Asp Gly Phe Arg Ile Lys Leu Tyr Phe Met His
    50                  55                  60
Phe Asn Leu Glu Ser Ser Tyr Leu Cys Glu Tyr Asp Tyr Val Lys Val
65                  70                  75                  80
Glu Thr Glu Asp Gln Val Leu Ala Thr Phe Cys Gly Arg Glu Thr Thr
                85                  90                  95
Asp Thr Glu Gln Thr Pro Gly Gln Glu Val Val Leu Ser Pro Gly Ser
            100                 105                 110
Phe Met Ser Ile Thr Phe Arg Ser Asp Phe Ser Asn Glu Glu Arg Phe
        115                 120                 125
Thr Gly Phe Asp Ala His Tyr Met Ala Val Asp Val Asp Glu Cys Lys
    130                 135                 140
Glu Arg Glu Asp Glu Glu Leu Ser Cys Asp His Tyr Cys His Asn Tyr
145                 150                 155                 160
Ile Gly Gly Tyr Tyr Cys Ser Cys Arg Phe Gly Tyr Ile Leu His Thr
                165                 170                 175
Asp Asn Arg Thr Cys Arg Val Glu Cys Ser Asp Asn Leu Phe Thr Gln
            180                 185                 190
Arg Thr Gly Val Ile Thr Ser Pro Asp Phe Pro Asn Pro Tyr Pro Lys
        195                 200                 205
Ser Ser Glu Cys Leu Tyr Thr Ile Glu Leu Glu Glu Gly Phe Met Val
    210                 215                 220
Asn Leu Gln Phe Glu Asp Ile Phe Asp Ile Gln Asp His Pro Glu Val
225                 230                 235                 240
Pro Cys Pro Tyr Asp Tyr Ile Lys Ile Lys Val Gly Pro Lys Val Leu
                245                 250                 255
Gly Pro Phe Cys Gly Glu Lys Ala Pro Glu Pro Ile Ser Thr Gln Ser
            260                 265                 270
His Ser Val Leu Ile Leu Phe His Ser Asp Asn Ser Ala Glu Asn Arg
        275                 280                 285
Gly Trp Arg Leu Ser Tyr Arg Ala Ala Gly Asn Glu Cys Pro Glu Leu
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Gln Pro Pro Val His Gly Lys Ile Glu Pro Ser Gln Ala Lys Tyr Phe
305                 310                 315                 320
Phe Lys Asp Gln Val Leu Val Ser Cys Asp Thr Gly Tyr Lys Val Leu
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Lys Asp Asn Val Glu Met Asp Thr Phe Gln Ile Glu Cys Leu Lys Asp
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        355                 360                 365
Ala Pro Gly Glu Leu Glu His Gly Leu Ile Thr Phe Ser Thr Arg Asn
    370                 375                 380
Asn Leu Thr Thr Tyr Lys Ser Glu Ile Lys Tyr Ser Cys Gln Glu Pro
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Tyr Tyr Lys Met Leu Asn Asn Asn Thr Gly Ile Tyr Thr Cys Ser Ala
                405                 410                 415
Gln Gly Val Trp Met Asn Lys Val Leu Gly Arg Ser Leu Pro Thr Cys
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Leu Pro Val Cys Gly Leu Pro Lys Phe Ser Arg Lys Leu Met Ala Arg
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Ile Phe Asn Gly Arg Pro Ala Gln Lys Gly Thr Thr Pro Trp Ile Ala
    450                 455                 460
Met Leu Ser His Leu Asn Gly Gln Pro Phe Cys Gly Gly Ser Leu Leu
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Gly Ser Ser Trp Ile Val Thr Ala Ala His Cys Leu His Gln Ser Leu
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Asp Pro Lys Asp Pro Thr Leu Arg Asp Ser Asp Leu Leu Ser Pro Ser
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Asp Phe Lys Ile Ile Leu Gly Lys His Trp Arg Leu Arg Ser Asp Glu
        515                 520                 525
Asn Glu Gln His Leu Gly Val Lys His Thr Thr Leu His Pro Gln Tyr
    530                 535                 540
Asp Pro Asn Thr Phe Glu Asn Asp Val Ala Leu Val Glu Leu Leu Glu
545                 550                 555                 560
Ser Pro Val Leu Asn Ala Phe Val Met Pro Ile Cys Leu Pro Glu Gly
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Pro Gln Gln Glu Gly Ala Met Val Ile Val Ser Gly Trp Gly Lys Gln
            580                 585                 590
Phe Leu Gln Arg Phe Pro Glu Thr Leu Met Glu Ile Glu Ile Pro Ile
        595                 600                 605
Val Asp His Ser Thr Cys Gln Lys Ala Tyr Ala Pro Leu Lys Lys Lys
    610                 615                 620
Val Thr Arg Asp Met Ile Cys Ala Gly Glu Lys Glu Gly Gly Lys Asp
625                 630                 635                 640
Ala Cys Ala Gly Asp Ser Gly Gly Pro Met Val Thr Leu Asn Arg Glu
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Arg Gly Gln Trp Tyr Leu Val Gly Thr Val Ser Trp Gly Asp Asp Cys
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Gly Lys Lys Asp Arg Tyr Gly Val Tyr Ser Tyr Ile His His Asn Lys
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<210> 327
<211> 4137
<212> DNA
<213> Homo sapiens

<400> 327

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<210> 328
<211> 728
<212> PRT

<213> Homo sapiens

<400> 328

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Asn Ile Thr Val Pro Asp Gly Phe Arg Ile Lys Leu Tyr Phe Met His
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Phe Asn Leu Glu Ser Ser Tyr Leu Cys Glu Tyr Asp Tyr Val Lys Val
65                  70                  75                  80
Glu Thr Glu Asp Gln Val Leu Ala Thr Phe Cys Gly Arg Glu Thr Thr
                85                  90                  95
Asp Thr Glu Gln Thr Pro Gly Gln Glu Val Val Leu Ser Pro Gly Ser
            100                 105                 110
Phe Met Ser Ile Thr Phe Arg Ser Asp Phe Ser Asn Glu Glu Arg Phe
        115                 120                 125
Thr Gly Phe Asp Ala His Tyr Met Ala Val Asp Val Asp Glu Cys Lys
    130                 135                 140
Glu Arg Glu Asp Glu Glu Leu Ser Cys Asp His Tyr Cys His Asn Tyr
145                 150                 155                 160
Ile Gly Gly Tyr Tyr Cys Ser Cys Arg Phe Gly Tyr Ile Leu His Thr
                165                 170                 175
Asp Asn Arg Thr Cys Arg Val Glu Cys Ser Asp Asn Leu Phe Thr Gln
            180                 185                 190
Arg Thr Gly Val Ile Thr Ser Pro Asp Phe Pro Asn Pro Tyr Pro Lys
        195                 200                 205
Ser Ser Glu Cys Leu Tyr Thr Ile Glu Leu Glu Glu Gly Phe Met Val
    210                 215                 220
Asn Leu Gln Phe Glu Asp Ile Phe Asp Ile Glu Asp His Pro Glu Val
225                 230                 235                 240
Pro Cys Pro Tyr Asp Tyr Ile Lys Ile Lys Val Gly Pro Lys Val Leu
                245                 250                 255
Gly Pro Phe Cys Gly Glu Lys Ala Pro Glu Pro Ile Ser Thr Gln Ser
            260                 265                 270
His Ser Val Leu Ile Leu Phe His Ser Asp Asn Ser Gly Glu Asn Arg
        275                 280                 285
Gly Trp Arg Leu Ser Tyr Arg Ala Ala Gly Asn Glu Cys Pro Glu Leu
    290                 295                 300
Gln Pro Pro Val His Gly Lys Ile Glu Pro Ser Gln Ala Lys Tyr Phe
305                 310                 315                 320
Phe Lys Asp Gln Val Leu Val Ser Cys Asp Thr Gly Tyr Lys Val Leu
                325                 330                 335
Lys Asp Asn Val Glu Met Asp Thr Phe Gln Ile Glu Cys Leu Lys Asp
            340                 345                 350
Gly Thr Trp Ser Asn Lys Ile Pro Thr Cys Lys Ile Val Asp Cys Arg
        355                 360                 365
Ala Pro Gly Glu Leu Glu His Gly Leu Ile Thr Phe Ser Thr Arg Asn
    370                 375                 380
Asn Leu Thr Thr Tyr Lys Ser Glu Ile Lys Tyr Ser Cys Gln Glu Pro
385                 390                 395                 400
Tyr Tyr Lys Met Leu Asn Asn Asn Thr Gly Ile Tyr Thr Cys Ser Ala
                405                 410                 415
Gln Gly Val Trp Met Asn Lys Val Leu Gly Arg Ser Leu Pro Thr Cys
            420                 425                 430
Leu Pro Glu Cys Gly Gln Pro Ser Arg Ser Leu Pro Ser Leu Val Lys
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        435                 440                 445
Arg Ile Ile Gly Gly Arg Asn Ala Glu Pro Gly Leu Phe Pro Trp Gln
    450                 455                 460
Ala Leu Ile Val Val Glu Asp Thr Ser Arg Val Pro Asn Asp Lys Trp
465                 470                 475                 480
Phe Gly Ser Gly Ala Leu Leu Ser Ala Ser Trp Ile Leu Thr Ala Ala
                485                 490                 495
His Val Leu Arg Ser Gln Arg Arg Asp Thr Thr Val Ile Pro Val Ser
            500                 505                 510
Lys Glu His Val Thr Val Tyr Leu Gly Leu His Asp Val Arg Asp Lys
        515                 520                 525
Ser Gly Ala Val Asn Ser Ser Ala Ala Arg Val Val Leu His Pro Asp
    530                 535                 540
Phe Asn Ile Gln Asn Tyr Asn His Asp Ile Ala Leu Val Gln Leu Gln
545                 550                 555                 560
Glu Pro Val Pro Leu Gly Pro His Val Met Pro Val Cys Leu Pro Arg
                565                 570                 575
Leu Glu Pro Glu Gly Pro Ala Pro His Met Leu Gly Leu Val Ala Gly
            580                 585                 590
Trp Gly Ile Ser Asn Pro Asn Val Thr Val Asp Glu Ile Ile Ser Ser
        595                 600                 605
Gly Thr Arg Thr Leu Ser Asp Val Leu Gln Tyr Val Lys Leu Pro Val
    610                 615                 620
Val Pro His Ala Glu Cys Lys Thr Ser Tyr Glu Ser Arg Ser Gly Asn
625                 630                 635                 640
Tyr Ser Val Thr Glu Asn Met Phe Cys Ala Gly Tyr Tyr Glu Gly Gly
                645                 650                 655
Lys Asp Thr Cys Leu Gly Asp Ser Gly Gly Ala Phe Val Ile Phe Asp
            660                 665                 670
Asp Leu Ser Gln Arg Trp Val Val Gln Gly Leu Val Ser Trp Gly Gly
        675                 680                 685
Pro Glu Glu Cys Gly Ser Lys Gln Val Tyr Gly Val Tyr Thr Lys Val
    690                 695                 700
Ser Asn Tyr Val Asp Trp Val Trp Glu Gln Met Gly Leu Pro Gln Ser
705                 710                 715                 720
Val Val Glu Pro Gln Val Glu Arg
                725
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<210> 329
<211> 2072
<212> DNA
<213> Homo sapiens

<400> 329

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gaggaaaagc cagagggaga gaggggaga ggggatctgt tgcaggcagg ggaaggcgtg 180
acctgaatgg agaatgccag ccaattccag agacacacag ggacctcaga acaaagataa 240
ggcatcacgg acaccacacc gggcacgagc tcacaggcaa gtcaagctgg gaggaccaag 300
gccgggcagc cgggagcacc caaggcagga aaatgaggtg gctgcttctc tattatgctc 360
tgtgcttctc cctgtcaaag gcttcagccc acaccgtgga gctaaacaat atgtttggcc 420
agatccagtc gcctggttat ccagactcct atcccagtga ttcagaggtg acttggaata 480
tcactgtccc agatgggttt cggatcaagc tttacttcat gcacttcaac ttggaatcct 540
cctacctttg tgaatatgac tatgtgaagg tagaaactga ggaccaggtg ctggcaacct 600
tctgtggcag ggagaccaca gacacagagc agactcccgg ccaggaggtg gtcctctccc 660
ctggctcctt catgtccatc actttccggt cagatttctc caatgaggag cgtttcacag 720
gctttgatgc ccactacatg gctgtggatg tggacgagtg caaggagagg gaggacgagg 780
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agctgtcctg tgaccactac tgccacaact acattggcgg ctactactgc tcctgccgct 840
tcggctacat cctccacaca gacaacagga cctgccgagt ggagtgcagt gacaacctct 900
tcactcaaag gactggggtg atcaccagcc ctgacttccc aaacccttac cccaagagct 960
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cccacaacac ccccgtgccc ctttccatgt ggattagaat gggtgctgaa caacatgatc 1620
tcagcagttg aagctgctac gtgtgtgaaa gcaaattctc cacttgaggg tttgcccatc 1680
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acatgtcaag tttaaatgaa ccagactgcc tgtgacttta tgaatctgaa ggtattacct 1920
gttgctgctt tcttaaccac catgagtagg taaagcaaat aataactcac agagtgtgga 1980
tttttgagaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 2072

<210> 330
<211> 380
<212> PRT
<213> Homo sapiens

<400> 330
Met Arg Trp Leu Leu Leu Tyr Tyr Ala Leu Cys Phe Ser Leu Ser Lys
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Ala Ser Ala His Thr Val Glu Leu Asn Asn Met Phe Gly Gln Ile Gln
20 25 30
Ser Pro Gly Tyr Pro Asp Ser Tyr Pro Ser Asp Ser Glu Val Thr Trp
35 40 45
Asn Ile Thr Val Pro Asp Gly Phe Arg Ile Lys Leu Tyr Phe Met His
50 55 60
Phe Asn Leu Glu Ser Ser Tyr Leu Cys Glu Tyr Asp Tyr Val Lys Val
65 70 75 80
Glu Thr Glu Asp Gln Val Leu Ala Thr Phe Cys Gly Arg Glu Thr Thr
85 90 95
Asp Thr Glu Gln Thr Pro Gly Gln Glu Val Val Leu Ser Pro Gly Ser
100 105 110
Phe Met Ser Ile Thr Phe Arg Ser Asp Phe Ser Asn Glu Glu Arg Phe
115 120 125
Thr Gly Phe Asp Ala His Tyr Met Ala Val Asp Val Asp Glu Cys Lys
130 135 140
Glu Arg Glu Asp Glu Glu Leu Ser Cys Asp His Tyr Cys His Asn Tyr
145 150 155 160
Ile Gly Gly Tyr Tyr Cys Ser Cys Arg Phe Gly Tyr Ile Leu His Thr
165 170 175
Asp Asn Arg Thr Cys Arg Val Glu Cys Ser Asp Asn Leu Phe Thr Gln
180 185 190
Arg Thr Gly Val Ile Thr Ser Pro Asp Phe Pro Asn Pro Tyr Pro Lys
195 200 205
Ser Ser Glu Cys Leu Tyr Thr Ile Glu Leu Glu Glu Gly Phe Met Val
210 215 220
Asn Leu Gln Phe Glu Asp Ile Phe Asp Ile Glu Asp His Pro Glu Val

```
225                 230                 235                 240
Pro Cys Pro Tyr Asp Tyr Ile Lys Ile Lys Val Gly Pro Lys Val Leu
                245                 250                 255
Gly Pro Phe Cys Gly Glu Lys Ala Pro Glu Pro Ile Ser Thr Gln Ser
            260                 265                 270
His Ser Val Leu Ile Leu Phe His Ser Asp Asn Ser Gly Glu Asn Arg
        275                 280                 285
Gly Trp Arg Leu Ser Tyr Arg Ala Ala Gly Asn Glu Cys Pro Glu Leu
    290                 295                 300
Gln Pro Pro Val His Gly Lys Ile Glu Pro Ser Gln Ala Lys Tyr Phe
305                 310                 315                 320
Phe Lys Asp Gln Val Leu Val Ser Cys Asp Thr Gly Tyr Lys Val Leu
                325                 330                 335
Lys Asp Asn Val Glu Met Asp Thr Phe Gln Ile Glu Cys Leu Lys Asp
            340                 345                 350
Gly Thr Trp Ser Asn Lys Ile Pro Thr Cys Lys Lys Asn Glu Ile Asp
        355                 360                 365
Leu Glu Ser Glu Leu Lys Ser Glu Gln Val Thr Glu
    370                 375                 380
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<210> 331
<211> 2460
<212> DNA
<213> Homo sapiens

<400> 331

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ggctttccag gggagtatgc caatgaccag gagcggcgct ggaccctgac tgcaccccca 180
ggctaccgcc tgcgcctcta cttcacccac ttcgacctgg agctctccca cctctgcgag 240
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gacattacct tccgctccga ctactccaac gagaagccgt tcacggggtt cgaggccttc 420
tatgcagccg aggacattga cgagtgccag gtggccccgg gagaggcgcc cacctgcgac 480
caccactgcc acaaccacct gggcggtttc tactgctcct gccgcgcagg ctacgtcctg 540
caccgtaaca agcgcacctg ctcagccctg tgctccggcc aggtcttcac ccagaggtct 600
ggggagctca gcagccctga atacccacgg ccgtatccca aactctccag ttgcacttac 660
agcatcagcc tggaggaggg gttcagtgtc attctggact ttgtggagtc cttcgatgtg 720
gagacacacc ctgaaaccct gtgtccctac gactttctca agattcaaac agacagagaa 780
gaacatggcc cattctgtgg gaagacattg ccccacagga ttgaaacaaa aagcaacacg 840
gtgaccatca cctttgtcac agatgaatca ggagaccaca caggctggaa gatccactac 900
acgagcacag cgcagccttg cccttatccg atggcgccac ctaatggcca cgtttcacct 960
gtgcaagcca aatacatcct gaaagacagc ttctccatct tttgcgagac tggctatgag 1020
cttctgcaag gtcacttgcc cctgaaatcc tttactgcag tttgtcagaa agatggatct 1080
tgggaccggc caatgcccgc gtgcagcatt gttgactgtg gccctcctga tgatctaccc 1140
agtggccgag tggagtacat cacaggtcct ggagtgacca cctacaaagc tgtgattcag 1200
tacagctgtg aagagacctt ctacacaatg aaagtgaatg atggtaaata tgtgtgtgag 1260
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gccctggaca ttcgaatggg caccctgaaa agactatcac ctcattatac acaagcctgg 1560
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ggattaaccc aaaggggttt tcttgctaga aatctaatgt atgtcgacat accgattgtt 1800
gaccatcaaa aatgtactgc tgcatatgaa aagccaccct atccaagggg aagtgtaact 1860
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tcctggggtt ccatgaattg tggggaagca ggtcagtatg gagtctacac aaaagttatt 2040
aactatattc cctggatcga gaacataatt agtgattttt aacttgcgtg tctgcagtca 2100
aggattcttc atttttagaa atgcctgtga agaccttggc agcgacgtgg ctcgagaagc 2160
attcatcatt actgtggaca tggcagttgt tgctccaccc aaaaaaaacag actccaggtg 2220
aggctgctgt catttctcca cttgccagtt taattccagc cttacccatt gactcaaggg 2280
gacataaacc acgagagtga cagtcatctt tgcccaccca gtgtaatgtc actgctcaaa 2340
ttacatttca ttaccttaaa aagccagtct cttttcatac tggctgttgg catttctgta 2400
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<210> 332
<211> 686
<212> PRT
<213> Homo sapiens

<400> 332

Met	Arg	Leu	Leu	Thr	Leu	Leu	Gly	Leu	Leu	Cys	Gly	Ser	Val	Ala	Thr
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Pro	Leu	Gly	Pro	Lys	Trp	Pro	Glu	Pro	Val	Phe	Gly	Arg	Leu	Ala	Ser
			20					25					30		
Pro	Gly	Phe	Pro	Gly	Glu	Tyr	Ala	Asn	Asp	Gln	Glu	Arg	Arg	Trp	Thr
		35					40					45			
Leu	Thr	Ala	Pro	Pro	Gly	Tyr	Arg	Leu	Arg	Leu	Tyr	Phe	Thr	His	Phe
	50					55					60				
Asp	Leu	Glu	Leu	Ser	His	Leu	Cys	Glu	Tyr	Asp	Phe	Val	Lys	Leu	Ser
65					70					75					80
Ser	Gly	Ala	Lys	Val	Leu	Ala	Thr	Leu	Cys	Gly	Gln	Glu	Ser	Thr	Asp
			85					90					95		
Thr	Glu	Arg	Ala	Pro	Gly	Lys	Asp	Thr	Phe	Tyr	Ser	Leu	Gly	Ser	Ser
		100					105					110			
Leu	Asp	Ile	Thr	Phe	Arg	Ser	Asp	Tyr	Ser	Asn	Glu	Lys	Pro	Phe	Thr
	115					120					125				
Gly	Phe	Glu	Ala	Phe	Tyr	Ala	Ala	Glu	Asp	Ile	Asp	Glu	Cys	Gln	Val
130					135					140					
Ala	Pro	Gly	Glu	Ala	Pro	Thr	Cys	Asp	His	His	Cys	His	Asn	His	Leu
145					150					155					160
Gly	Gly	Phe	Tyr	Cys	Ser	Cys	Arg	Ala	Gly	Tyr	Val	Leu	His	Arg	Asn
				165					170					175	
Lys	Arg	Thr	Cys	Ser	Ala	Leu	Cys	Ser	Gly	Gln	Val	Phe	Thr	Gln	Arg
			180					185					190		
Ser	Gly	Glu	Leu	Ser	Ser	Pro	Glu	Tyr	Pro	Arg	Pro	Tyr	Pro	Lys	Leu
		195					200					205			
Ser	Ser	Cys	Thr	Tyr	Ser	Ile	Ser	Leu	Glu	Glu	Gly	Phe	Ser	Val	Ile
	210					215					220				
Leu	Asp	Phe	Val	Glu	Ser	Phe	Asp	Val	Glu	Thr	His	Pro	Glu	Thr	Leu
225					230					235					240
Cys	Pro	Tyr	Asp	Phe	Leu	Lys	Ile	Gln	Thr	Asp	Arg	Glu	Glu	His	Gly
				245					250					255	
Pro	Phe	Cys	Gly	Lys	Thr	Leu	Pro	His	Arg	Ile	Glu	Thr	Lys	Ser	Asn
			260					265					270		
Thr	Val	Thr	Ile	Thr	Phe	Val	Thr	Asp	Glu	Ser	Gly	Asp	His	Thr	Gly
		275					280					285			
Trp	Lys	Ile	His	Tyr	Thr	Ser	Thr	Ala	His	Ala	Cys	Pro	Tyr	Pro	Met
	290					295					300				
Ala	Pro	Pro	Asn	Gly	His	Val	Ser	Pro	Val	Gln	Ala	Lys	Tyr	Ile	Leu
305					310					315					320

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Lys Asp Ser Phe Ser Ile Phe Cys Glu Thr Gly Tyr Glu Leu Leu Gln
                325                 330                 335
Gly His Leu Pro Leu Lys Ser Phe Thr Ala Val Cys Gln Lys Asp Gly
            340                 345                 350
Ser Trp Asp Arg Pro Met Pro Ala Cys Ser Ile Val Asp Cys Gly Pro
        355                 360                 365
Pro Asp Asp Leu Pro Ser Gly Arg Val Glu Tyr Ile Thr Gly Pro Gly
    370                 375                 380
Val Thr Thr Tyr Lys Ala Val Ile Gln Tyr Ser Cys Glu Glu Thr Phe
385                 390                 395                 400
Tyr Thr Met Lys Val Asn Asp Gly Lys Tyr Val Cys Glu Ala Asp Gly
                405                 410                 415
Phe Trp Thr Ser Ser Lys Gly Glu Lys Ser Leu Pro Val Cys Glu Pro
            420                 425                 430
Val Cys Gly Leu Ser Ala Arg Thr Thr Gly Gly Arg Ile Tyr Gly Gly
        435                 440                 445
Gln Lys Ala Lys Pro Gly Asp Phe Pro Trp Gln Val Leu Ile Leu Gly
    450                 455                 460
Gly Thr Thr Ala Ala Gly Ala Leu Leu Tyr Asp Asn Trp Val Leu Thr
465                 470                 475                 480
Ala Ala His Ala Val Tyr Glu Gln Lys His Asp Ala Ser Ala Leu Asp
                485                 490                 495
Ile Arg Met Gly Thr Leu Lys Arg Leu Ser Pro His Tyr Thr Gln Ala
            500                 505                 510
Trp Ser Glu Ala Val Phe Ile His Glu Gly Tyr Thr His Asp Ala Gly
        515                 520                 525
Phe Asp Asn Asp Ile Ala Leu Ile Lys Leu Asn Asn Lys Val Val Ile
    530                 535                 540
Asn Ser Asn Ile Thr Pro Ile Cys Leu Pro Arg Lys Glu Ala Glu Ser
545                 550                 555                 560
Phe Met Arg Thr Asp Asp Ile Gly Thr Ala Ser Gly Trp Gly Leu Thr
                565                 570                 575
Gln Arg Gly Phe Leu Ala Arg Asn Leu Met Tyr Val Asp Ile Pro Ile
            580                 585                 590
Val Asp His Gln Lys Cys Thr Ala Ala Tyr Glu Lys Pro Pro Tyr Pro
        595                 600                 605
Arg Gly Ser Val Thr Ala Asn Met Leu Cys Ala Gly Leu Glu Ser Gly
    610                 615                 620
Gly Lys Asp Ser Cys Arg Gly Asp Ser Gly Gly Ala Leu Val Phe Leu
625                 630                 635                 640
Asp Ser Glu Thr Glu Arg Trp Phe Val Gly Gly Ile Val Ser Trp Gly
                645                 650                 655
Ser Met Asn Cys Gly Glu Ala Gly Gln Tyr Gly Val Tyr Thr Lys Val
            660                 665                 670
Ile Asn Tyr Ile Pro Trp Ile Glu Asn Ile Ile Ser Asp Phe
        675                 680                 685
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<210> 333
<211> 738
<212> DNA
<213> Homo sapiens

<400> 333
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ggctttccag gggagtatgc caatgaccag gagcggcgct ggaccctgac tgcacccccc 180
ggctaccgcc tgcgcctcta cttcacccac ttcgacctgg agctctccca cctctgcgag 240

tacgacttcg tcaagctgag ctcgggggcc aaggtgctgg ccacgctgtg cgggcaggag 300
agcacagaca cggagcgggc ccctggcaag gacactttct actcgctggg ctccagcctg 360
gacattacct tccgctccga ctactccaac gagaagccgt tcacggggtt cgaggccttc 420
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caccactgcc acaaccacct gggcggtttc tactgctcct gccgcgcagg ctacgtcctg 540
caccgtaaca agcgcacctg ctcagagcag agcctctagc ctcccctgga gctccggcct 600
gcccagcagg tcagaagcca gagccagcct gctggcctca gctccgggtt gggctgagat 660
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aaaaaaaaaa aaaaaaaa 738

<210> 334
<211> 185
<212> PRT
<213> Homo sapiens

<400> 334
Met Arg Leu Leu Thr Leu Leu Gly Leu Leu Cys Gly Ser Val Ala Thr
1 5 10 15
Pro Leu Gly Pro Lys Trp Pro Glu Pro Val Phe Gly Arg Leu Ala Ser
20 25 30
Pro Gly Phe Pro Gly Glu Tyr Ala Asn Asp Gln Glu Arg Arg Trp Thr
35 40 45
Leu Thr Ala Pro Pro Gly Tyr Arg Leu Arg Leu Tyr Phe Thr His Phe
50 55 60
Asp Leu Glu Leu Ser His Leu Cys Glu Tyr Asp Phe Val Lys Leu Ser
65 70 75 80
Ser Gly Ala Lys Val Leu Ala Thr Leu Cys Gly Gln Glu Ser Thr Asp
85 90 95
Thr Glu Arg Ala Pro Gly Lys Asp Thr Phe Tyr Ser Leu Gly Ser Ser
100 105 110
Leu Asp Ile Thr Phe Arg Ser Asp Tyr Ser Asn Glu Lys Pro Phe Thr
115 120 125
Gly Phe Glu Ala Phe Tyr Ala Ala Glu Asp Ile Asp Glu Cys Gln Val
130 135 140
Ala Pro Gly Glu Ala Pro Thr Cys Asp His His Cys His Asn His Leu
145 150 155 160
Gly Gly Phe Tyr Cys Ser Cys Arg Ala Gly Tyr Val Leu His Arg Asn
165 170 175
Lys Arg Thr Cys Ser Glu Gln Ser Leu
180 185

<210> 335
<211> 248
<212> PRT
<213> Homo sapiens

<400> 335
Met Ser Leu Phe Pro Ser Leu Pro Leu Leu Leu Leu Ser Met Val Ala
1 5 10 15
Ala Ser Tyr Ser Glu Thr Val Thr Cys Glu Asp Ala Gln Lys Thr Cys
20 25 30
Pro Ala Val Ile Ala Cys Ser Ser Pro Gly Ile Asn Gly Phe Pro Gly
35 40 45
Lys Asp Gly Arg Asp Gly Thr Lys Gly Glu Lys Gly Glu Pro Gly Gln
50 55 60
Gly Leu Arg Gly Leu Gln Gly Pro Pro Gly Lys Leu Gly Pro Pro Gly
65 70 75 80

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Asn Pro Gly Pro Ser Gly Ser Pro Gly Pro Lys Gly Gln Lys Gly Asp
                85                  90                  95
Pro Gly Lys Ser Pro Asp Gly Asp Ser Ser Leu Ala Ala Ser Glu Arg
            100                 105                 110
Lys Ala Leu Gln Thr Glu Met Ala Arg Ile Lys Lys Trp Leu Thr Phe
        115                 120                 125
Ser Leu Gly Lys Gln Val Gly Asn Lys Phe Phe Leu Thr Asn Gly Glu
    130                 135                 140
Ile Met Thr Phe Glu Lys Val Lys Ala Leu Cys Val Lys Phe Gln Ala
145                 150                 155                 160
Ser Val Ala Thr Pro Arg Asn Ala Ala Glu Asn Gly Ala Ile Gln Asn
                165                 170                 175
Leu Ile Lys Glu Glu Ala Phe Leu Gly Ile Thr Asp Glu Lys Thr Glu
            180                 185                 190
Gly Gln Phe Val Asp Leu Thr Gly Asn Arg Leu Thr Tyr Thr Asn Trp
        195                 200                 205
Asn Glu Gly Glu Pro Asn Asn Ala Gly Ser Asp Glu Asp Cys Val Leu
    210                 215                 220
Leu Leu Lys Asn Gly Gln Trp Asn Asp Val Pro Cys Ser Thr Ser His
225                 230                 235                 240
Leu Ala Val Cys Glu Phe Pro Ile
                245
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<210> 336
<211> 392
<212> PRT
<213> Homo sapiens

<400> 336

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            20                  25                  30
Asp Ala Cys Glu Glu Pro Pro Thr Phe Glu Ala Met Glu Leu Ile Gly
        35                  40                  45
Lys Pro Lys Pro Tyr Tyr Glu Ile Gly Glu Arg Val Asp Tyr Lys Cys
    50                  55                  60
Lys Lys Gly Tyr Phe Tyr Ile Pro Pro Leu Ala Thr His Thr Ile Cys
65                  70                  75                  80
Asp Arg Asn His Thr Trp Leu Pro Val Ser Asp Asp Ala Cys Tyr Arg
                85                  90                  95
Glu Thr Cys Pro Tyr Ile Arg Asp Pro Leu Asn Gly Gln Ala Val Pro
            100                 105                 110
Ala Asn Gly Thr Tyr Glu Phe Gly Tyr Gln Met His Phe Ile Cys Asn
        115                 120                 125
Glu Gly Tyr Tyr Leu Ile Gly Glu Glu Ile Leu Tyr Cys Glu Leu Lys
    130                 135                 140
Gly Ser Val Ala Ile Trp Ser Gly Lys Pro Pro Ile Cys Glu Lys Val
145                 150                 155                 160
Leu Cys Thr Pro Pro Pro Lys Ile Lys Asn Gly Lys His Thr Phe Ser
                165                 170                 175
Glu Val Glu Val Phe Glu Tyr Leu Asp Ala Val Thr Tyr Ser Cys Asp
            180                 185                 190
Pro Ala Pro Gly Pro Asp Pro Phe Ser Leu Ile Gly Glu Ser Thr Ile
        195                 200                 205
Tyr Cys Gly Asp Asn Ser Val Trp Ser Arg Ala Ala Pro Glu Cys Lys
    210                 215                 220
```

```
Val Val Lys Cys Arg Phe Pro Val Val Glu Asn Gly Lys Gln Ile Ser
225                 230                 235                 240
Gly Phe Gly Lys Lys Phe Tyr Tyr Lys Ala Thr Val Met Phe Glu Cys
                245                 250                 255
Asp Lys Gly Phe Tyr Leu Asp Gly Ser Asp Thr Ile Val Cys Asp Ser
            260                 265                 270
Asn Ser Thr Trp Asp Pro Pro Val Pro Lys Cys Leu Lys Val Leu Pro
        275                 280                 285
Pro Ser Ser Thr Lys Pro Pro Ala Leu Ser His Ser Val Ser Thr Ser
    290                 295                 300
Ser Thr Thr Lys Ser Pro Ala Ser Ser Ala Ser Gly Pro Arg Pro Thr
305                 310                 315                 320
Tyr Lys Pro Pro Val Ser Asn Tyr Pro Gly Tyr Pro Lys Pro Glu Glu
                325                 330                 335
Gly Ile Leu Asp Ser Leu Asp Val Trp Val Ile Ala Val Ile Val Ile
            340                 345                 350
Ala Ile Val Val Gly Val Ala Val Ile Cys Val Val Pro Tyr Arg Tyr
        355                 360                 365
Leu Gln Arg Arg Lys Lys Lys Gly Thr Tyr Leu Thr Asp Glu Thr His
    370                 375                 380
Arg Glu Val Lys Phe Thr Ser Leu
385                 390
```

<210> 337
<211> 2574
<212> DNA
<213> Homo sapiens

<400> 337

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ctaggtctgg agtttcagct tggacactga gccaagcaga caagcaaagc aagccaggac 180
acaccatcct gccccaggcc cagcttctct cctgccttcc aacgccatgg ggagcaatct 240
cagcccccaa ctctgcctga tgccctttat cttgggcctc ttgtctggag gtgtgaccac 300
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gaagccaaga tatggtctag tgacatatgc cacataccca aaaatttggg tcaaagtgtc 1200
tgaagcagac agcagtaatg cagactgggt cacgaagcag ctcaatgaaa tcaattatga 1260
agaccacaag ttgaagtcag ggactaacac caagaaggcc ctccaggcag tgtacagcat 1320
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cctcatgact gatggattgc acaacatggg cggggaccca attactgtca ttgatgagat 1440
ccgggacttg ctatacattg gcaaggatcg caaaaaccca agggaggatt atctggatgt 1500
ctatgtgttt ggggtcgggc ctttggtgaa ccaagtgaac atcaatgctt tggcttccaa 1560
gaaagacaat gagcaacatg tgttcaaagt caaggatatg gaaaacctgg aagatgtttt 1620
ctaccaaatg atcgatgaaa gccagtctct gagtctctgt ggcatggttt gggaacacag 1680
```

```
gaagggtacc gattaccaca agcaaccatg gcaggccaag atctcagtca ttcgcccttc 1740
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acattgtttc actgtggatg acaaggaaca ctcaatcaag gtcagcgtag gaggggagaa 1860
gcgggacctg gagatagaag tagtcctatt tcaccccaac tacaacatta atgggaaaaa 1920
agaagcagga attcctgaat tttatgacta tgacgttgcc ctgatcaagc tcaagaataa 1980
gctgaaatat ggccagacta tcaggcccat ttgtctcccc tgcaccgagg gaacaactcg 2040
agctttgagg cttcctccaa ctaccacttg ccagcaacaa aaggaagagc tgctccctgc 2100
acaggatatc aaagctctgt ttgtgtctga ggaggagaaa aagctgactc ggaaggaggt 2160
ctacatcaag aatggggata agaaaggcag ctgtgagaga gatgctcaat atgccccagg 2220
ctatgacaaa gtcaaggaca tctcagaggt ggtcaccct cggttccttt gtactggagg 2280
agtgagtccc tatgctgacc ccaatacttg cagaggtgat tctggcggcc ccttgatagt 2340
tcacaagaga agtcgtttca ttcaagttgg tgtaatcagc tggggagtag tggatgtctg 2400
caaaaaccag aagcggcaaa agcaggtacc tgctcacgcc cgagactttc acatcaacct 2460
ctttcaagtg ctgccctggc tgaaggagaa actccaagat gaggatttgg gttttctata 2520
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```

<210> 338
<211> 764
<212> PRT
<213> Homo sapiens

<400> 338

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Gly Leu Leu Ser Gly Gly Val Thr Thr Thr Pro Trp Ser Leu Ala Arg
            20                  25                  30
Pro Gln Gly Ser Cys Ser Leu Glu Gly Val Glu Ile Lys Gly Gly Ser
        35                  40                  45
Phe Arg Leu Leu Gln Glu Gly Gln Ala Leu Glu Tyr Val Cys Pro Ser
    50                  55                  60
Gly Phe Tyr Pro Tyr Pro Val Gln Thr Arg Thr Cys Arg Ser Thr Gly
65                  70                  75                  80
Ser Trp Ser Thr Leu Lys Thr Gln Asp Gln Lys Thr Val Arg Lys Ala
                85                  90                  95
Glu Cys Arg Ala Ile His Cys Pro Arg Pro His Asp Phe Glu Asn Gly
            100                 105                 110
Glu Tyr Trp Pro Arg Ser Pro Tyr Tyr Asn Val Ser Asp Glu Ile Ser
        115                 120                 125
Phe His Cys Tyr Asp Gly Tyr Thr Leu Arg Gly Ser Ala Asn Arg Thr
    130                 135                 140
Cys Gln Val Asn Gly Arg Trp Ser Gly Gln Thr Ala Ile Cys Asp Asn
145                 150                 155                 160
Gly Ala Gly Tyr Cys Ser Asn Pro Gly Ile Pro Ile Gly Thr Arg Lys
                165                 170                 175
Val Gly Ser Gln Tyr Arg Leu Glu Asp Ser Val Thr Tyr His Cys Ser
            180                 185                 190
Arg Gly Leu Thr Leu Arg Gly Ser Gln Arg Arg Thr Cys Gln Glu Gly
        195                 200                 205
Gly Ser Trp Ser Gly Thr Glu Pro Ser Cys Gln Asp Ser Phe Met Tyr
    210                 215                 220
Asp Thr Pro Gln Glu Val Ala Glu Ala Phe Leu Ser Ser Leu Thr Glu
225                 230                 235                 240
Thr Ile Glu Gly Val Asp Ala Glu Asp Gly His Gly Pro Gly Glu Gln
                245                 250                 255
Gln Lys Arg Lys Ile Val Leu Asp Pro Ser Gly Ser Met Asn Ile Tyr
            260                 265                 270
Leu Val Leu Asp Gly Ser Asp Ser Ile Gly Ala Ser Asn Phe Thr Gly
        275                 280                 285
```

```
Ala Lys Lys Cys Leu Val Asn Leu Ile Glu Lys Val Ala Ser Tyr Gly
    290                 295                 300
Val Lys Pro Arg Tyr Gly Leu Val Thr Tyr Ala Thr Tyr Pro Lys Ile
305                 310                 315                 320
Trp Val Lys Val Ser Glu Ala Asp Ser Ser Asn Ala Asp Trp Val Thr
                325                 330                 335
Lys Gln Leu Asn Glu Ile Asn Tyr Glu Asp His Lys Leu Lys Ser Gly
            340                 345                 350
Thr Asn Thr Lys Lys Ala Leu Gln Ala Val Tyr Ser Met Met Ser Trp
        355                 360                 365
Pro Asp Asp Val Pro Pro Glu Gly Trp Asn Arg Thr Arg His Val Ile
    370                 375                 380
Ile Leu Met Thr Asp Gly Leu His Asn Met Gly Gly Asp Pro Ile Thr
385                 390                 395                 400
Val Ile Asp Glu Ile Arg Asp Leu Leu Tyr Ile Gly Lys Asp Arg Lys
                405                 410                 415
Asn Pro Arg Glu Asp Tyr Leu Asp Val Tyr Val Phe Gly Val Gly Pro
            420                 425                 430
Leu Val Asn Gln Val Asn Ile Asn Ala Leu Ala Ser Lys Lys Asp Asn
        435                 440                 445
Glu Gln His Val Phe Lys Val Lys Asp Met Glu Asn Leu Glu Asp Val
    450                 455                 460
Phe Tyr Gln Met Ile Asp Glu Ser Gln Ser Leu Ser Leu Cys Gly Met
465                 470                 475                 480
Val Trp Glu His Arg Lys Gly Thr Asp Tyr His Lys Gln Pro Trp Gln
                485                 490                 495
Ala Lys Ile Ser Val Ile Arg Pro Ser Lys Gly His Glu Ser Cys Met
            500                 505                 510
Gly Ala Val Val Ser Glu Tyr Phe Val Leu Thr Ala Ala His Cys Phe
        515                 520                 525
Thr Val Asp Asp Lys Glu His Ser Ile Lys Val Ser Val Gly Gly Glu
    530                 535                 540
Lys Arg Asp Leu Glu Ile Glu Val Val Leu Phe His Pro Asn Tyr Asn
545                 550                 555                 560
Ile Asn Gly Lys Lys Glu Ala Gly Ile Pro Glu Phe Tyr Asp Tyr Asp
                565                 570                 575
Val Ala Leu Ile Lys Leu Lys Asn Lys Leu Lys Tyr Gly Gln Thr Ile
            580                 585                 590
Arg Pro Ile Cys Leu Pro Cys Thr Glu Gly Thr Thr Arg Ala Leu Arg
        595                 600                 605
Leu Pro Pro Thr Thr Thr Cys Gln Gln Gln Lys Glu Glu Leu Leu Pro
    610                 615                 620
Ala Gln Asp Ile Lys Ala Leu Phe Val Ser Glu Glu Glu Lys Lys Leu
625                 630                 635                 640
Thr Arg Lys Glu Val Tyr Ile Lys Asn Gly Asp Lys Lys Gly Ser Cys
                645                 650                 655
Glu Arg Asp Ala Gln Tyr Ala Pro Gly Tyr Asp Lys Val Lys Asp Ile
            660                 665                 670
Ser Glu Val Val Thr Pro Arg Phe Leu Cys Thr Gly Gly Val Ser Pro
        675                 680                 685
Tyr Ala Asp Pro Asn Thr Cys Arg Gly Asp Ser Gly Gly Pro Leu Ile
    690                 695                 700
Val His Lys Arg Ser Arg Phe Ile Gln Val Gly Val Ile Ser Trp Gly
705                 710                 715                 720
Val Val Asp Val Cys Lys Asn Gln Lys Arg Gln Lys Gln Val Pro Ala
                725                 730                 735
His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Trp Leu
            740                 745                 750
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Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu
755 760

<210> 339
<211> 1173
<212> DNA
<213> Homo sapiens

<400> 339
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cctaggagcg gccgcctgcg cggcgccgcc ccgtggtcgg atcctgggcg gcagagaggc 120
cgaggcgcac gcgcggccct acatggcgtc ggtgcagctg aacggcgcgc acctgtgcgg 180
cggcgtcctg gtggcggagc agtgggtgct gagcgcggcg cactgcctgg aggacgcggc 240
cgacgggaag gtgcaggttc tcctgggcgc gcactccctg tcgcagccgg agccctccaa 300
gcgcctgtac gacgtgctcc gcgcagtgcc ccacccggac agccagcccg acaccatcga 360
ccacgacctc ctgctgctac agctgtcgga gaaggccaca ctgggccctg ctgtgcgccc 420
cctgccctgg cagcgcgtgg accgcgacgt ggcaccggga actctctgcg acgtggccgg 480
ctggggcata gtcaaccacg cgggccgccg cccggacagc ctgcagcacg tgctcttgcc 540
agtgctggac cgcgccacct gcaaccggcg cacgcaccac gacggcgcca tcaccgagcg 600
cttgatgtgc gcggagagca atcgccggga cagctgcaag ggtgactccg ggggcccgct 660
ggtgtgcggg ggcgtgctcg agggcgtggt cacctcgggc tcgcgcgttt gcggcaaccg 720
caagaagccc gggatctaca cccgcgtggc gagctatgcg gcctggatcg acagcgtcct 780
ggcctagggt gccggggcct gaaggtcagg gtcacccaag caacaaagtc ccgagcaatg 840
aagtcatcca ctcctgcatc tggttggtct ttattgagca cctactatat gcagaagggg 900
aggccgaggt gggaggatca ttggatctca ggagttcgag atcagcatgg gccacgtagc 960
gcgactccat ctctacaaat aaataaaaaa ttagctgggc aattggcggg catggaggtg 1020
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accttgtctc tctctacaaa aaaaaaaaaa aaa 1173

<210> 340
<211> 253
<212> PRT
<213> Homo sapiens

<400> 340
Met His Ser Ser Val Tyr Phe Ala Val Leu Val Leu Leu Gly Ala Ala
1 5 10 15
Ala Cys Ala Ala Arg Pro Arg Gly Arg Ile Leu Gly Gly Arg Glu Ala
20 25 30
Glu Ala His Ala Arg Pro Tyr Met Ala Ser Val Gln Leu Asn Gly Ala
35 40 45
His Leu Cys Gly Gly Val Leu Val Ala Glu Gln Trp Val Leu Ser Ala
50 55 60
Ala His Cys Leu Glu Asp Ala Ala Asp Gly Lys Val Gln Val Leu Leu
65 70 75 80
Gly Ala His Ser Leu Ser Gln Pro Glu Pro Ser Lys Arg Leu Tyr Asp
85 90 95
Val Leu Arg Ala Val Pro His Pro Asp Ser Gln Pro Asp Thr Ile Asp
100 105 110
His Asp Leu Leu Leu Leu Gln Leu Ser Glu Lys Ala Thr Leu Gly Pro
115 120 125
Ala Val Arg Pro Leu Pro Trp Gln Arg Val Asp Arg Asp Val Ala Pro
130 135 140
Gly Thr Leu Cys Asp Val Ala Gly Trp Gly Ile Val Asn His Ala Gly
145 150 155 160
Arg Arg Pro Asp Ser Leu Gln His Val Leu Leu Pro Val Leu Asp Arg

```
                165                 170                 175
Ala Thr Cys Asn Arg Arg Thr His His Asp Gly Ala Ile Thr Glu Arg
            180                 185                 190
Leu Met Cys Ala Glu Ser Asn Arg Arg Asp Ser Cys Lys Gly Asp Ser
        195                 200                 205
Gly Gly Pro Leu Val Cys Gly Gly Val Leu Glu Gly Val Val Thr Ser
    210                 215                 220
Gly Ser Arg Val Cys Gly Asn Arg Lys Lys Pro Gly Ile Tyr Thr Arg
225                 230                 235                 240
Val Ala Ser Tyr Ala Ala Trp Ile Asp Ser Val Leu Ala
                245                 250
```

<210> 341
<211> 4004
<212> DNA
<213> Homo sapiens

<400> 341

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caaagattat ttgccttatg ttatgggcta tttgtgtagc agaagattgc aatgaacttc 180
ctccaagaag aaatacagaa attctgacag gttcctggtc tgaccaaaca tatccagaag 240
gcacccaggc tatctataaa tgccgccctg gatatagatc tcttggaaat gtaataatgg 300
tatgcaggaa gggagaatgg gttgctctta atccattaag gaaatgtcag aaaaggccct 360
gtggacatcc tggagatact ccttttggta cttttaccct tacaggagga aatgtgtttg 420
aatatggtgt aaaagctgtg tatacatgta atgaggggta tcaattgcta ggtgagatta 480
attaccgtga atgtgacaca gatggatgga ccaatgatat tcctatatgt gaagttgtga 540
agtgtttacc agtgacagca ccagagaatg gaaaaattgt cagtagtgca atggaaccag 600
atcgggaata ccatttgga caagcagtac ggtttgtatg taactcaggc tacaagattg 660
aaggagatga agaaatgcat tgttcagacg atggtttttg gagtaaagag aaaccaaagt 720
gtgtggaaat ttcatgcaaa tccccagatg ttataaatgg atctcctata tctcagaaga 780
ttatttataa ggagaatgaa cgatttcaat ataaatgtaa catgggttat gaatacagtg 840
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aatcatgtga taatccttat attccaaatg gtgactactc acctttaagg attaaacaca 960
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agtttgtaca gggtaaatct atagacgttg cctgccatcc tggctacgct cttccaaaag 1380
cgcagaccac agttacatgt atggagaatg gctggtctcc tactcccaga tgcatccgtg 1440
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cttcccctcc ttattactat ggagattcag tggaattcaa ttgctcagaa tcatttacaa 2280
tgattggaca cagatcaatt acgtgtattc atggagtatg gacccaactt ccccagtgtg 2340
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```
tggcaataga taaacttaag aagtgcaaat catcaaattt aattatactt gaggaacatt 2400
taaaaaacaa gaaggaattc gatcataatt ctaacataag gtacagatgt agaggaaaag 2460
aaggatggat acacacagtc tgcataaatg gaagatggga tccagaagtg aactgctcaa 2520
tggcacaaat acaattatgc ccacctccac ctcagattcc caattctcac aatatgacaa 2580
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cgtaaaattt tggattaatt tgtgaaaatg taattataag ctgagaccgg tggctctctt 3960
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<210> 342
<211> 1231
<212> PRT
<213> Homo sapiens

<400> 342

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Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys
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Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile
            20                  25                  30
Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala
        35                  40                  45
Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met
    50                  55                  60
Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys
65                  70                  75                  80
Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe
                85                  90                  95
Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr
            100                 105                 110
Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu
        115                 120                 125
Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val
    130                 135                 140
Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser
145                 150                 155                 160
Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe
                165                 170                 175
Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys
```

```
                180                 185                 190
Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile
        195                 200                 205
Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys
    210                 215                 220
Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly
225                 230                 235                 240
Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp
                245                 250                 255
Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr Ile
            260                 265                 270
Pro Asn Gly Asp Tyr Ser Pro Leu Arg Ile Lys His Arg Thr Gly Asp
        275                 280                 285
Glu Ile Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg Gly
    290                 295                 300
Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg Cys
305                 310                 315                 320
Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr
                325                 330                 335
His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr
            340                 345                 350
Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr
        355                 360                 365
Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro
    370                 375                 380
Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln
385                 390                 395                 400
Asn His Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys
                405                 410                 415
His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met
            420                 425                 430
Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys
        435                 440                 445
Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln
    450                 455                 460
Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu Gly
465                 470                 475                 480
Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Arg Cys Gly Lys
                485                 490                 495
Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile Pro
            500                 505                 510
Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys Leu
        515                 520                 525
Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn Thr
    530                 535                 540
Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser Asp
545                 550                 555                 560
Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp Val
                565                 570                 575
His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu Val
            580                 585                 590
Leu Lys Phe Ser Cys Lys Pro Gly Phe Thr Ile Val Gly Pro Asn Ser
        595                 600                 605
Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys
    610                 615                 620
Glu Gln Val Gln Ser Cys Gly Pro Pro Pro Glu Leu Leu Asn Gly Asn
625                 630                 635                 640
Val Lys Glu Lys Thr Lys Glu Glu Tyr Gly His Ser Glu Val Val Glu
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645 650 655
Tyr Tyr Cys Asn Pro Arg Phe Leu Met Lys Gly Pro Asn Lys Ile Gln
660 665 670
Cys Val Asp Gly Glu Trp Thr Thr Leu Pro Val Cys Ile Val Glu Glu
675 680 685
Ser Thr Cys Gly Asp Ile Pro Glu Leu Glu His Gly Trp Ala Gln Leu
690 695 700
Ser Ser Pro Pro Tyr Tyr Tyr Gly Asp Ser Val Glu Phe Asn Cys Ser
705 710 715 720
Glu Ser Phe Thr Met Ile Gly His Arg Ser Ile Thr Cys Ile His Gly
725 730 735
Val Trp Thr Gln Leu Pro Gln Cys Val Ala Ile Asp Lys Leu Lys Lys
740 745 750
Cys Lys Ser Ser Asn Leu Ile Ile Leu Glu Glu His Leu Lys Asn Lys
755 760 765
Lys Glu Phe Asp His Asn Ser Asn Ile Arg Tyr Arg Cys Arg Gly Lys
770 775 780
Glu Gly Trp Ile His Thr Val Cys Ile Asn Gly Arg Trp Asp Pro Glu
785 790 795 800
Val Asn Cys Ser Met Ala Gln Ile Gln Leu Cys Pro Pro Pro Pro Gln
805 810 815
Ile Pro Asn Ser His Asn Met Thr Thr Thr Leu Asn Tyr Arg Asp Gly
820 825 830
Glu Lys Val Ser Val Leu Cys Gln Glu Asn Tyr Leu Ile Gln Glu Gly
835 840 845
Glu Glu Ile Thr Cys Lys Asp Gly Arg Trp Gln Ser Ile Pro Leu Cys
850 855 860
Val Glu Lys Ile Pro Cys Ser Gln Pro Pro Gln Ile Glu His Gly Thr
865 870 875 880
Ile Asn Ser Ser Arg Ser Ser Gln Glu Ser Tyr Ala His Gly Thr Lys
885 890 895
Leu Ser Tyr Thr Cys Glu Gly Gly Phe Arg Ile Ser Glu Glu Asn Glu
900 905 910
Thr Thr Cys Tyr Met Gly Lys Trp Ser Ser Pro Pro Gln Cys Glu Gly
915 920 925
Leu Pro Cys Lys Ser Pro Pro Glu Ile Ser His Gly Val Val Ala His
930 935 940
Met Ser Asp Ser Tyr Gln Tyr Gly Glu Glu Val Thr Tyr Lys Cys Phe
945 950 955 960
Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu
965 970 975
Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu
980 985 990
Pro Ser Phe Glu Asn Ala Ile Pro Met Gly Glu Lys Lys Asp Val Tyr
995 1000 1005
Lys Ala Gly Glu Gln Val Thr Tyr Thr Cys Ala Thr Tyr Tyr Lys Met
1010 1015 1020
Asp Gly Ala Ser Asn Val Thr Cys Ile Asn Ser Arg Trp Thr Gly Arg
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Pro Thr Cys Arg Asp Thr Ser Cys Val Asn Pro Pro Thr Val Gln Asn
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Ala Tyr Ile Val Ser Arg Gln Met Ser Lys Tyr Pro Ser Gly Glu Arg
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Val Arg Tyr Gln Cys Arg Ser Pro Tyr Glu Met Phe Gly Asp Glu Glu
1075 1080 1085
Val Met Cys Leu Asn Gly Asn Trp Thr Glu Pro Pro Gln Cys Lys Asp
1090 1095 1100
Ser Thr Gly Lys Cys Gly Pro Pro Pro Pro Ile Asp Asn Gly Asp Ile

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1105                1110                1115                1120
Thr Ser Phe Pro Leu Ser Val Tyr Ala Pro Ala Ser Ser Val Glu Tyr
                1125                1130                1135
Gln Cys Gln Asn Leu Tyr Gln Leu Glu Gly Asn Lys Arg Ile Thr Cys
            1140                1145                1150
Arg Asn Gly Gln Trp Ser Glu Pro Pro Lys Cys Leu His Pro Cys Val
        1155                1160                1165
Ile Ser Arg Glu Ile Met Glu Asn Tyr Asn Ile Ala Leu Arg Trp Thr
    1170                1175                1180
Ala Lys Gln Lys Leu Tyr Ser Arg Thr Gly Glu Ser Val Glu Phe Val
1185                1190                1195                1200
Cys Lys Arg Gly Tyr Arg Leu Ser Ser Arg Ser His Thr Leu Arg Thr
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Thr Cys Trp Asp Gly Lys Leu Glu Tyr Pro Thr Cys Ala Lys Arg
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<210> 343
<211> 1701
<212> DNA
<213> Homo sapiens

<400> 343

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acccaaggtc acacggctag gaagttgctg cacgctccta tgctccattt cctctgggag 180
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ctgcctttgc ctaccagaaa cgtagtggtg ggctctgtca gccttgcagg tccccacgat 480
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<210> 344
<211> 469
<212> PRT
<213> Homo sapiens

<400> 344

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            20                  25                  30
Phe Thr Gln Tyr Glu Glu Ser Ser Gly Lys Cys Lys Gly Leu Leu Gly
        35                  40                  45
Gly Gly Val Ser Val Glu Asp Cys Cys Leu Asn Thr Ala Phe Ala Tyr
    50                  55                  60
Gln Lys Arg Ser Gly Gly Leu Cys Gln Pro Cys Arg Ser Pro Arg Trp
65                  70                  75                  80
Ser Leu Trp Ser Thr Trp Ala Pro Cys Ser Val Thr Cys Ser Glu Gly
                85                  90                  95
Ser Gln Leu Arg Tyr Arg Arg Cys Val Gly Trp Asn Gly Gln Cys Ser
            100                 105                 110
Gly Lys Val Ala Pro Gly Thr Leu Glu Trp Gln Leu Gln Ala Cys Glu
        115                 120                 125
Asp Gln Gln Cys Cys Pro Glu Met Gly Gly Trp Ser Gly Trp Gly Pro
    130                 135                 140
Trp Glu Pro Cys Ser Val Thr Cys Ser Lys Gly Thr Arg Thr Arg Arg
145                 150                 155                 160
Arg Ala Cys Asn His Pro Ala Pro Lys Cys Gly Gly His Cys Pro Gly
                165                 170                 175
Gln Ala Gln Glu Ser Glu Ala Cys Asp Thr Gln Gln Val Cys Pro Thr
            180                 185                 190
His Gly Ala Trp Ala Thr Trp Gly Pro Trp Thr Pro Cys Ser Ala Ser
        195                 200                 205
Cys His Gly Gly Pro His Glu Pro Lys Glu Thr Arg Ser Arg Lys Cys
    210                 215                 220
Ser Ala Pro Glu Pro Ser Gln Lys Pro Pro Gly Lys Pro Cys Pro Gly
225                 230                 235                 240
Leu Ala Tyr Glu Gln Arg Arg Cys Thr Gly Leu Pro Pro Cys Pro Val
                245                 250                 255
Ala Gly Gly Trp Gly Pro Trp Gly Pro Val Ser Pro Cys Pro Val Thr
            260                 265                 270
Cys Gly Leu Gly Gln Thr Met Glu Gln Arg Thr Cys Asn His Pro Val
        275                 280                 285
Pro Gln His Gly Gly Pro Phe Cys Ala Gly Asp Ala Thr Arg Thr His
    290                 295                 300
Ile Cys Asn Thr Ala Val Pro Cys Pro Val Asp Gly Glu Trp Asp Ser
305                 310                 315                 320
Trp Gly Glu Trp Ser Pro Cys Ile Arg Arg Asn Met Lys Ser Ile Ser
                325                 330                 335
Cys Gln Glu Ile Pro Gly Gln Gln Ser Arg Gly Arg Thr Cys Arg Gly
            340                 345                 350
Arg Lys Phe Asp Gly His Arg Cys Ala Gly Gln Gln Gln Asp Ile Arg
        355                 360                 365
His Cys Tyr Ser Ile Gln His Cys Pro Leu Lys Gly Ser Trp Ser Glu
    370                 375                 380
Trp Ser Thr Trp Gly Leu Cys Met Pro Pro Cys Gly Pro Asn Pro Thr
385                 390                 395                 400
Arg Ala Arg Gln Arg Leu Cys Thr Pro Leu Leu Pro Lys Tyr Pro Pro
                405                 410                 415
Thr Val Ser Met Val Glu Gly Gln Gly Glu Lys Asn Val Thr Phe Trp
            420                 425                 430
Gly Arg Pro Leu Pro Arg Cys Glu Glu Leu Gln Gly Gln Lys Leu Val
        435                 440                 445
Val Glu Glu Lys Arg Pro Cys Leu His Val Pro Ala Cys Lys Asp Pro
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450 455 460
Glu Glu Glu Glu Leu
465

<210> 345
<211> 3462
<212> DNA
<213> Artificial Sequence

<220>
<223> Vector: pQE32

<400> 345
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ggatctcacc atcaccatca ccatgggatc cgcatgcgag ctcggtaccc cgggtcgacc 180
tgcagccaag cttaattagc tgagcttgga ctcctgttga tagatccagt aatgacctca 240
gaactccatc tggatttgtt cagaacgctc ggttgccgcc gggcgttttt tattggtgag 300
aatccaagct agcttggcga gattttcagg agctaaggaa gctaaaatgg agaaaaaaat 360
cactggatat accaccgttg atatatccca atggcatcgt aaagaacatt ttgaggcatt 420
tcagtcagtt gctcaatgta cctataacca gaccgttcag ctggatatta cggccttttt 480
aaagaccgta aagaaaaata agcacaagtt ttatccggcc tttattcaca ttcttgcccg 540
cctgatgaat gctcatccgg aatttcgtat ggcaatgaaa gacggtgagc tggtgatatg 600
ggatagtgtt cacccttgtt acaccgtttt ccatgagcaa actgaaacgt tttcatcgct 660
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<210> 346
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Dforward

<400> 346
cacccttct tcaatgacga caccttcgac tatgacatcg 40

<210> 347
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Dreverse

<400> 347
cgatgtcata gtcgaaggtg tcgtcattga agaaggggtg 40

<210> 348
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Eforward

<400> 348
ccacccttc ttcaatgacg agaccttcga ctatgacatc gc 42

<210> 349
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Ereverse

<400> 349
gcgatgtcat agtcgaaggt ctcgtcattg aagaaggggt gg 42

<210> 350
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Aforward

<400> 350
cacccttct tcaatgacgc caccttcgac tatgacatc 39

<210> 351
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: F97Areverse

<400> 351
gatgtcatag tcgaaggtgg cgtcattgaa gaaggggtg 39

<210> 352
<211> 39
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<220>
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<400> 352
cacccttct tcaatgactg gaccttcgac tatgacatc 39

<210> 353
<211> 39
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<220>
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<400> 353
gatgtcatag tcgaaggtcc agtcattgaa gaaggggtg 39

<210> 354
<211> 27
<212> DNA
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<220>
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<400> 354
ggacacaccc agaacggagg cactggc 27

<210> 355
<211> 27

<212> DNA
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<220>
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<400> 355
gccagtgcct ccgttctggg tgtgtcc 27

<210> 356
<211> 27
<212> DNA
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<220>
<223> Primer: Y146Dforward

<400> 356
ggacacaccc aggacggagg cactggc 27

<210> 357
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Dreverse

<400> 357
gccagtgcct ccgtcctggg tgtgtcc 27

<210> 358
<211> 29
<212> DNA
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<220>
<223> Primer: Y146Eforward

<400> 358
gggacacacc caggagggag gcactggcg 29

<210> 359
<211> 29
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<220>
<223> Primer: Y146Ereverse

<400> 359
cgccagtgcc tccctcctgg gtgtgtccc 29

<210> 360
<211> 29
<212> DNA
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<220>
<223> Primer: Y146Aforward

<400> 360
gggacacacc caggccggag gcactggcg 29

<210> 361
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Areverse

<400> 361
cgccagtgcc tccggcctgg gtgtgtccc 29

<210> 362
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Wforward

<400> 362
gggacacacc cagtggggag gcactggcg 29

<210> 363
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Wreverse

<400> 363
cgccagtgcc tccccactgg gtgtgtccc 29

<210> 364
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Rforward

<400> 364
ggggacacac ccagagggga ggcactggcg c 31

<210> 365
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Y146Rreverse

<400> 365
gcgccagtgc ctcccctctg ggtgtgtccc c 31

<210> 366
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Q192Rforward

<400> 366
tggactcctg ccggggtgat tccgg 25

<210> 367
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: Q192Rreverse

<400> 367
ccggaatcac cccggcagga gtcca 25

<210> 368
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: K224Aforward

<400> 368
cgctcagagg aacgcgccag gcgtgtaca 29

<210> 369
<211> 29
<212> DNA
<213> Homo sapiens

<220>
<223> Primer: K224Areverse

<400> 369
tgtacacgcc tggcgcgttc ctctgagcg 29

<210> 370
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: K224Fforward

<400> 370
gctgcgctca gaggaacttc ccaggcgtgt acacaag 37

<210> 371
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer: K224Freverse

<400> 371
cttgtgtaca cgcctgggaa gttcctctga gcgcagc 37

<210> 372
<211> 1575
<212> DNA
<213> Homo sapiens

<400> 372
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cgcggtcgag taggtgtgca ccagccctgg caacgagagc gtctaccccg aactctgctg 180
gccttgaggt ggggaagccg gggagggcag ttgaggaccc cgcggaggcg cgtgactggt 240
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tttaatttca aatgt 1575

<210> 373
<211> 333
<212> PRT
<213> Homo sapiens

<400> 373
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Ala Thr Leu Thr Phe Asp His Ser Leu Glu Ala Gln Trp Thr Lys Trp
20 25 30
Lys Ala Met His Asn Arg Leu Tyr Gly Met Asn Glu Glu Gly Trp Arg
35 40 45
Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gln

```
    50                  55                  60
Glu Tyr Arg Glu Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe
65                  70                  75                  80
Gly Asp Met Thr Ser Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln
                85                  90                  95
Asn Arg Lys Pro Arg Lys Gly Lys Val Phe Gln Glu Pro Leu Phe Tyr
            100                 105                 110
Glu Ala Pro Arg Ser Val Asp Trp Arg Glu Lys Gly Tyr Val Thr Pro
        115                 120                 125
Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr
    130                 135                 140
Gly Ala Leu Glu Gly Gln Met Phe Arg Lys Thr Gly Arg Leu Ile Ser
145                 150                 155                 160
Leu Ser Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu
                165                 170                 175
Gly Cys Asn Gly Gly Leu Met Asp Tyr Ala Phe Gln Tyr Val Gln Asp
            180                 185                 190
Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu
        195                 200                 205
Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly
    210                 215                 220
Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala
225                 230                 235                 240
Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe
                245                 250                 255
Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu
            260                 265                 270
Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr
        275                 280                 285
Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu
    290                 295                 300
Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn
305                 310                 315                 320
His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val
                325                 330
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<210> 374
<211> 1342
<212> DNA
<213> Homo sapiens

<400> 374

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cggctgtaat ctcagaggct tgtttgctga gggtgcctgc gcacgtgcga cggctgctgg 60
ttttgaaaca tgaatctttc gctcgtcctg gctgcctttt gcttgggaat agcctccgct 120
gttccaaaat ttgaccaaaa tttggataca aagtggtacc agtggaaggc aacacacaga 180
agattatatg gcgcgaatga agaaggatgg aggagagcag tgtgggaaaa gaatatgaaa 240
atgattgaac tgcacaatgg ggaatacagc caagggaaac atggcttcac aatggccatg 300
aatgcttttc ctgacatgac caatgaagaa ttcaggcaga tgatgggttg ctttcgaaac 360
cagaaattca ggaaggggaa agtgttccgt gagcctctgt ttcttgatct tcccaaatct 420
gtggattgga gaaagaaagg ctacgtgacg ccagtgaaga atcagaaaca gtgtggttct 480
tgttgggctt ttagtgcgac tggtgctctt gaaggacaga tgttccggaa aactgggaaa 540
cttgtctcac tgagcgagca gaatctggtg gactgttcgc gtcctcaagg caatcagggc 600
tgcaatggtg gcttcatggc tagggccttc cagtatgtca aggagaacgg aggcctggac 660
tctgaggaat cctatccata tgtagcagtg gatgaaatct gtaagtacag acctgagaat 720
tctgttgcta atgacactgg cttcacagtg gtcgcacctg gaaaggagaa ggccctgatg 780
aaagcagtcg caactgtggg gcccatctcc gttgctatgg atgcaggcca ttcgtccttc 840
cagttctaca aatcaggcat ttattttgaa ccagactgca gcagcaaaaa cctggatcat 900
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ggtgttctgg tggttggcta cggctttgaa ggagcaaatt cgaataacag caagtattgg 960
ctcgtcaaaa acagctgggg tccagaatgg ggctcgaatg gctatgtaaa aatagccaaa 1020
gacaagaaca accactgtgg aatcgccaca gcagccagct accccaatgt gtgagctgat 1080
ggatggtgag gaggaaggac ttaaggacag catgtctggg gaaatttttat cttgaaactg 1140
accaaacgct tattgtgtaa gataaaccag ttgaatcatt gaggatccaa gttgagattt 1200
taattctgtg acatttttac aagggtaaaa tgttaccact actttaatta ttgttataca 1260
cagctttatg atatcaaaga ctcattgctt aattctaaga cttttgaatt ttcatttttt 1320
aaaaagatgt acaaaacagt tt 1342

<210> 375
<211> 334
<212> PRT
<213> Homo sapiens

<400> 375

Met	Asn	Leu	Ser	Leu	Val	Leu	Ala	Ala	Phe	Cys	Leu	Gly	Ile	Ala	Ser
1				5				10					15		
Ala	Val	Pro	Lys	Phe	Asp	Gln	Asn	Leu	Asp	Thr	Lys	Trp	Tyr	Gln	Trp
			20					25					30		
Lys	Ala	Thr	His	Arg	Arg	Leu	Tyr	Gly	Ala	Asn	Glu	Glu	Gly	Trp	Arg
		35					40					45			
Arg	Ala	Val	Trp	Glu	Lys	Asn	Met	Lys	Met	Ile	Glu	Leu	His	Asn	Gly
	50					55					60				
Glu	Tyr	Ser	Gln	Gly	Lys	His	Gly	Phe	Thr	Met	Ala	Met	Asn	Ala	Phe
65					70					75					80
Gly	Asp	Met	Thr	Asn	Glu	Glu	Phe	Arg	Gln	Met	Met	Gly	Cys	Phe	Arg
				85					90					95	
Asn	Gln	Lys	Phe	Arg	Lys	Gly	Lys	Val	Phe	Arg	Glu	Pro	Leu	Phe	Leu
			100					105					110		
Asp	Leu	Pro	Lys	Ser	Val	Asp	Trp	Arg	Lys	Lys	Gly	Tyr	Val	Thr	Pro
		115					120					125			
Val	Lys	Asn	Gln	Lys	Gln	Cys	Gly	Ser	Cys	Trp	Ala	Phe	Ser	Ala	Thr
	130					135					140				
Gly	Ala	Leu	Glu	Gly	Gln	Met	Phe	Arg	Lys	Thr	Gly	Lys	Leu	Val	Ser
145					150					155					160
Leu	Ser	Glu	Gln	Asn	Leu	Val	Asp	Cys	Ser	Arg	Pro	Gln	Gly	Asn	Gln
				165					170					175	
Gly	Cys	Asn	Gly	Gly	Phe	Met	Ala	Arg	Ala	Phe	Gln	Tyr	Val	Lys	Glu
			180					185					190		
Asn	Gly	Gly	Leu	Asp	Ser	Glu	Glu	Ser	Tyr	Pro	Tyr	Val	Ala	Val	Asp
		195					200					205			
Glu	Ile	Cys	Lys	Tyr	Arg	Pro	Glu	Asn	Ser	Val	Ala	Asn	Asp	Thr	Gly
	210					215					220				
Phe	Thr	Val	Val	Ala	Pro	Gly	Lys	Glu	Lys	Ala	Leu	Met	Lys	Ala	Val
225					230					235					240
Ala	Thr	Val	Gly	Pro	Ile	Ser	Val	Ala	Met	Asp	Ala	Gly	His	Ser	Ser
				245					250					255	
Phe	Gln	Phe	Tyr	Lys	Ser	Gly	Ile	Tyr	Phe	Glu	Pro	Asp	Cys	Ser	Ser
			260					265					270		
Lys	Asn	Leu	Asp	His	Gly	Val	Leu	Val	Val	Gly	Tyr	Gly	Phe	Glu	Gly
		275					280					285			
Ala	Asn	Ser	Asn	Asn	Ser	Lys	Tyr	Trp	Leu	Val	Lys	Asn	Ser	Trp	Gly
	290					295					300				
Pro	Glu	Trp	Gly	Ser	Asn	Gly	Tyr	Val	Lys	Ile	Ala	Lys	Asp	Lys	Asn
305					310					315					320
Asn	His	Cys	Gly	Ile	Ala	Thr	Ala	Ala	Ser	Tyr	Pro	Asn	Val		
				325					330						

<210> 376
<211> 1661
<212> DNA
<213> Homo sapiens

<400> 376
attcggcacg agccgcaatc ccgatggaat aaatctagca cccctgatgg tgtgcccaca 60
ctttgctgcc gaaacgaagc cagacaacag atttccatca gcaggatgtg ggggctcaag 120
gttctgctgc tacctgtggt gagctttgct ctgtaccctg aggagatact ggacacccac 180
tgggagctat ggaagaagac ccacaggaag caatataaca acaaggtgga tgaaatctct 240
cggcgtttaa tttgggaaaa aaacctgaag tatatttcca tccataacct tgaggcttct 300
cttggtgtcc atacatatga actggctatg aaccacctgg gggacatgac cagtgaagag 360
gtggttcaga agatgactgg actcaaagta cccctgtctc attcccgcag taatgacacc 420
ctttatatcc cagaatggga aggtagagcc ccagactctg tcgactatcg aaagaaagga 480
tatgttactc ctgtcaaaaa tcagggtcag tgtggttcct gttgggcttt tagctctgtg 540
ggtgccctgg agggccaact caagaagaaa actggcaaac tcttaaatct gagtccccag 600
aacctagtgg attgtgtgtc tgagaatgat ggctgtggag ggggctacat gaccaatgcc 660
ttccaatatg tgcagaagaa ccggggtatt gactctgaag atgcctaccc atatgtggga 720
caggaagaga gttgtatgta caacccaaca ggcaaggcag ctaaatgcag agggtacaga 780
gagatccccg aggggaatga gaaagccctg aagagggcag tggcccgagt gggacctgtc 840
tctgtggcca ttgatgcaag cctgacctcc ttccagtttt acagcaaagg tgtgtattat 900
gatgaaagct gcaatagcga taatctgaac catgcggttt tggcagtggg atatggaatc 960
cagaagggaa acaagcactg gataattaaa aacagctggg gagaaaactg gggaaacaaa 1020
ggatatatcc tcatggctcg aaataagaac aacgcctgtg gcattgccaa cctggccagc 1080
ttccccaaga tgtgactcca gccagccaaa tccatcctgc tcttccattt cttccacgat 1140
ggtgcagtgt aacgatgcac tttggaaggg agttggtgtg ctatttttga agcagatgtg 1200
gtgatactga gattgtctgt tcagtttccc catttgtttg tgcttcaaat gatccttcct 1260
actttggttc tctcctccca tgacctttt cactgtggcc atcaggactt tccctgacag 1320
ctgtgtactc ttaggctaag agatgtgact acagcctgcc cctgactgtg ttgtcccagg 1380
gctgatgctg tacaggtaca ggctggagat tttcacatag gttagattct cattcacggg 1440
actagttagc tttaagcacc ctagaggact agggtaatct gacttctcac ttcctaagtt 1500
cccttcaata tcctcaaggt agaaatgtct atgttttcta ctccaattca taaatctatt 1560
cataagtctt tggtacaagt ttacatgata aaaagaaatg tgatttgtct tcccttcttt 1620
gcacttttga aataaagtat ttatctcctg tctacagttt a 1661

<210> 377
<211> 329
<212> PRT
<213> Homo sapiens

<400> 377
Met Trp Gly Leu Lys Val Leu Leu Leu Pro Val Val Ser Phe Ala Leu
 1   5   10   15
Tyr Pro Glu Glu Ile Leu Asp Thr His Trp Glu Leu Trp Lys Lys Thr
            20   25   30
His Arg Lys Gln Tyr Asn Asn Lys Val Asp Glu Ile Ser Arg Arg Leu
        35   40   45
Ile Trp Glu Lys Asn Leu Lys Tyr Ile Ser Ile His Asn Leu Glu Ala
    50   55   60
Ser Leu Gly Val His Thr Tyr Glu Leu Ala Met Asn His Leu Gly Asp
65   70   75   80
Met Thr Ser Glu Glu Val Val Gln Lys Met Thr Gly Leu Lys Val Pro
                85   90   95
Leu Ser His Ser Arg Ser Asn Asp Thr Leu Tyr Ile Pro Glu Trp Glu
            100   105   110
Gly Arg Ala Pro Asp Ser Val Asp Tyr Arg Lys Lys Gly Tyr Val Thr
        115   120   125

```
Pro Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ser
    130                 135                 140
Val Gly Ala Leu Glu Gly Gln Leu Lys Lys Lys Thr Gly Lys Leu Leu
145                 150                 155                 160
Asn Leu Ser Pro Gln Asn Leu Val Asp Cys Val Ser Glu Asn Asp Gly
                165                 170                 175
Cys Gly Gly Gly Tyr Met Thr Asn Ala Phe Gln Tyr Val Gln Lys Asn
            180                 185                 190
Arg Gly Ile Asp Ser Glu Asp Ala Tyr Pro Tyr Val Gly Gln Glu Glu
        195                 200                 205
Ser Cys Met Tyr Asn Pro Thr Gly Lys Ala Ala Lys Cys Arg Gly Tyr
    210                 215                 220
Arg Glu Ile Pro Glu Gly Asn Glu Lys Ala Leu Lys Arg Ala Val Ala
225                 230                 235                 240
Arg Val Gly Pro Val Ser Val Ala Ile Asp Ala Ser Leu Thr Ser Phe
                245                 250                 255
Gln Phe Tyr Ser Lys Gly Val Tyr Tyr Asp Glu Ser Cys Asn Ser Asp
            260                 265                 270
Asn Leu Asn His Ala Val Leu Ala Val Gly Tyr Gly Ile Gln Lys Gly
        275                 280                 285
Asn Lys His Trp Ile Ile Lys Asn Ser Trp Gly Glu Asn Trp Gly Asn
    290                 295                 300
Lys Gly Tyr Ile Leu Met Ala Arg Asn Lys Asn Asn Ala Cys Gly Ile
305                 310                 315                 320
Ala Asn Leu Ala Ser Phe Pro Lys Met
                325
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<210> 378
<211> 1255
<212> DNA
<213> Homo sapiens

<400> 378
ctaaagatga aacggctggt ttgtgtgctc ttggtgtgct cctctgcagt ggcacagttg 60
cataaagatc ctaccctgga tcaccactgg catctctgga agaaaaccta tggcaaacaa 120
tacaaggaaa agaatgaaga agcagtacga cgtctcatct gggaaaagaa tctaaagttt 180
gtgatgcttc acaacctgga gcattcaatg ggaatgcact catacgatct gggcatgaac 240
cacctgggag acatgaccag tgaagaagtg atgtctttga cgagttccct gagagttccc 300
agccagtggc agagaaatat cacatataag tcaaacccta atcggatatt gcctgattct 360
gtggactgga gagagaaagg gtgtgttact gaagtgaaat atcaaggttc ttgtggtgct 420
tgctgggctt tcagtgctgt gggggccctg gaagcacagc tgaagctgaa aacaggaaag 480
ctggtgactc tcagtgccca gaacctggtg gattgctcaa ctgaaaaata tggaaacaaa 540
ggctgcaatg gtggcttcat gacaacggct ttccagtaca tcattgataa caagggcatc 600
gactcagacg cttcctatcc ctacaaagcc atggatcaga aatgtcaata tgactcaaaa 660
tatcgtgctg ccacatgttc aaagtacact gaacttcctt atgggagaga agatgtcctg 720
aaagaagctg tggccaataa aggcccagtg tctgttggtg tagatgcgcg tcatccttct 780
ttcttcctct acagaagtgg tgtctactat gaaccatcct gtactcagaa tgtgaatcat 840
ggtgtacttg tggttggcta tggtgatctt aatgggaaag aatactggct tgtgaaaaac 900
agctggggcc acaactttgg tgaagaagga tatattcgga tggcaagaaa taaaggaaat 960
cattgtggga ttgctagctt tccctcttac ccagaaatct agaggatctc tccttttttat 1020
aacaaatcaa gaaatatgaa gcactttctc ttaacttaat ttttcctgct gtatccagaa 1080
gaaataattg tgtcatgatt aatgtgtatt tactgtacta atagaaaata tagtttgagg 1140
ccgggcactg tctggctcac gcctgtaatc ccagtacttg ggaggccaag gaggcatatc 1200
aacttgaggc caggagttaa agagcagcct ggctaactgt gaaaccctct ctact 1255

<210> 379
<211> 331

<212> PRT
<213> Homo sapiens

<400> 379

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Met Lys Arg Leu Val Cys Val Leu Leu Val Cys Ser Ser Ala Val Ala
 1               5                  10                  15
Gln Leu His Lys Asp Pro Thr Leu Asp His His Trp His Leu Trp Lys
            20                  25                  30
Lys Thr Tyr Gly Lys Gln Tyr Lys Glu Lys Asn Glu Glu Ala Val Arg
        35                  40                  45
Arg Leu Ile Trp Glu Lys Asn Leu Lys Phe Val Met Leu His Asn Leu
    50                  55                  60
Glu His Ser Met Gly Met His Ser Tyr Asp Leu Gly Met Asn His Leu
65                  70                  75                  80
Gly Asp Met Thr Ser Glu Glu Val Met Ser Leu Met Ser Ser Leu Arg
                85                  90                  95
Val Pro Ser Gln Trp Gln Arg Asn Ile Thr Tyr Lys Ser Asn Pro Asn
            100                 105                 110
Arg Ile Leu Pro Asp Ser Val Asp Trp Arg Glu Lys Gly Cys Val Thr
        115                 120                 125
Glu Val Lys Tyr Gln Gly Ser Cys Gly Ala Cys Trp Ala Phe Ser Ala
    130                 135                 140
Val Gly Ala Leu Glu Ala Gln Leu Lys Leu Lys Thr Gly Lys Leu Val
145                 150                 155                 160
Thr Leu Ser Ala Gln Asn Leu Val Asp Cys Ser Thr Glu Lys Tyr Gly
                165                 170                 175
Asn Lys Gly Cys Asn Gly Gly Phe Met Thr Thr Ala Phe Gln Tyr Ile
            180                 185                 190
Ile Asp Asn Lys Gly Ile Asp Ser Asp Ala Ser Tyr Pro Tyr Lys Ala
        195                 200                 205
Met Asp Gln Lys Cys Gln Tyr Asp Ser Lys Tyr Arg Ala Ala Thr Cys
    210                 215                 220
Ser Lys Tyr Thr Glu Leu Pro Tyr Gly Arg Glu Asp Val Leu Lys Glu
225                 230                 235                 240
Ala Val Ala Asn Lys Gly Pro Val Ser Val Gly Val Asp Ala Arg His
                245                 250                 255
Pro Ser Phe Phe Leu Tyr Arg Ser Gly Val Tyr Tyr Glu Pro Ser Cys
            260                 265                 270
Thr Gln Asn Val Asn His Gly Val Leu Val Val Gly Tyr Gly Asp Leu
        275                 280                 285
Asn Gly Lys Glu Tyr Trp Leu Val Lys Asn Ser Trp Gly His Asn Phe
    290                 295                 300
Gly Glu Glu Gly Tyr Ile Arg Met Ala Arg Asn Lys Gly Asn His Cys
305                 310                 315                 320
Gly Ile Ala Ser Phe Pro Ser Tyr Pro Glu Ile
                325                 330
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<210> 380
<211> 1517
<212> DNA
<213> Homo sapiens

<400> 380

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gaattccggg tctgttgggt ccgggccgcc ggcttcgccc tcgccatggc gccctggctg 60
cagctcctgt cgctgctggg gctgctcccg ggcgcagtgg ccgcccccgc ccagccccga 120
gccgccagct ttcaggcctg ggggccgccg tccccggagc tgctggcgcc cacccgcttc 180
gcgctggaga tgttcaaccg cggccgggct gcgggggacgc gggccgtgct gggccttgtg 240
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cgcggccgcg tccgccgggc gggtcagggg tcgctgtact ccctggaggc caccctggag 300
gagccaccct gcaacgaccc catggtgtgc cggctccccg tgtccaagaa aaccctgctc 360
tgcagcttcc aagtcctgga tgagctcgga agacacgtgc tgctgcggaa ggactgtggc 420
ccagtggaca ccaaggttcc aggtgctggg gagcccaagt cagccttcac tcagggctca 480
gccatgattt cttctctgtc ccaaaaccat ccagacaaca gaaacgagac tttcagctca 540
gtcatttccc tgttgaatga ggatcccctg tcccaggact tgcctgtgaa gatggcttca 600
atcttcaaga actttgtcat tacctataac cggacatatg agtcaaagga agaagcccgg 660
tggcgcctgt ccgtctttgt caataacatg gtgcgagcac agaagatcca ggccctggac 720
cgtgggacag ctcagtatgg agtcaccaag ttcagtgatc tcacagagga ggagttccgc 780
actatctacc tgaatactct cctgaggaaa gagcctggca acaagatgaa gcaagccaag 840
tctgtgggtg acctcgcccc acctgaatgg gactggagga gtaagggggc tgtcacaaaa 900
gtcaaagacc agggcatgtg tggctcctgc tgggccttct cagtcacagg caatgtggag 960
ggccagtggt ttctcaacca ggggaccctg ctctcccctct ctgaacagga gctcttggac 1020
tgtgacaaga tggacaaggc ctgcatgggc ggcttgccct ccaatgccta ctcggccata 1080
aagaatttgg gagggctgga gacagaggat gactacagct accagggtca catgcagtcc 1140
tgcaacttct cagcagagaa ggccaaggtc tacatcaatg actccgtgga gctgagccag 1200
aacgagcaga agctggcagc ctggctggcc aagagaggcc caatctccgt ggccatcaat 1260
gcctttggca tgcagtttta ccgccacggg atctcccgcc ctctccggcc cctctgcagc 1320
ccttggctca ttgaccatgc ggtgttgctt gtgggctacg gcaaccgctc tgacgttccc 1380
ttttgggcca tcaagaacag ctggggcact gactggggtg agaagggtta ctactacttg 1440
catcgtgggt ccggggcctg tggcgtgaac accatggcca gctcggcggt ggtggactga 1500
agaggggccc cgaattc                                                 1517

<210> 381
<211> 484
<212> PRT
<213> Homo sapiens

<400> 381
Met Ala Pro Trp Leu Gln Leu Leu Ser Leu Leu Gly Leu Leu Pro Gly
 1               5                  10                  15
Ala Val Ala Ala Pro Ala Gln Pro Arg Ala Ala Ser Phe Gln Ala Trp
            20                  25                  30
Gly Pro Pro Ser Pro Glu Leu Leu Ala Pro Thr Arg Phe Ala Leu Glu
        35                  40                  45
Met Phe Asn Arg Gly Arg Ala Ala Gly Thr Arg Ala Val Leu Gly Leu
    50                  55                  60
Val Arg Gly Arg Val Arg Arg Ala Gly Gln Gly Ser Leu Tyr Ser Leu
65                  70                  75                  80
Glu Ala Thr Leu Glu Glu Pro Pro Cys Asn Asp Pro Met Val Cys Arg
                85                  90                  95
Leu Pro Val Ser Lys Lys Thr Leu Leu Cys Ser Phe Gln Val Leu Asp
            100                 105                 110
Glu Leu Gly Arg His Val Leu Leu Arg Lys Asp Cys Gly Pro Val Asp
        115                 120                 125
Thr Lys Val Pro Gly Ala Gly Glu Pro Lys Ser Ala Phe Thr Gln Gly
    130                 135                 140
Ser Ala Met Ile Ser Ser Leu Ser Gln Asn His Pro Asp Asn Arg Asn
145                 150                 155                 160
Glu Thr Phe Ser Ser Val Ile Ser Leu Leu Asn Glu Asp Pro Leu Ser
                165                 170                 175
Gln Asp Leu Pro Val Lys Met Ala Ser Ile Phe Lys Asn Phe Val Ile
            180                 185                 190
Thr Tyr Asn Arg Thr Tyr Glu Ser Lys Glu Glu Ala Arg Trp Arg Leu
        195                 200                 205
Ser Val Phe Val Asn Asn Met Val Arg Ala Gln Lys Ile Gln Ala Leu
    210                 215                 220
Asp Arg Gly Thr Ala Gln Tyr Gly Val Thr Lys Phe Ser Asp Leu Thr
```

225 230 235 240
Glu Glu Glu Phe Arg Thr Ile Tyr Leu Asn Thr Leu Leu Arg Lys Glu
245 250 255
Pro Gly Asn Lys Met Lys Gln Ala Lys Ser Val Gly Asp Leu Ala Pro
260 265 270
Pro Glu Trp Asp Trp Arg Ser Lys Gly Ala Val Thr Lys Val Lys Asp
275 280 285
Gln Gly Met Cys Gly Ser Cys Trp Ala Phe Ser Val Thr Gly Asn Val
290 295 300
Glu Gly Gln Trp Phe Leu Asn Gln Gly Thr Leu Leu Ser Leu Ser Glu
305 310 315 320
Gln Glu Leu Leu Asp Cys Asp Lys Met Asp Lys Ala Cys Met Gly Gly
325 330 335
Leu Pro Ser Asn Ala Tyr Ser Ala Ile Lys Asn Leu Gly Gly Leu Glu
340 345 350
Thr Glu Asp Asp Tyr Ser Tyr Gln Gly His Met Gln Ser Cys Asn Phe
355 360 365
Ser Ala Glu Lys Ala Lys Val Tyr Ile Asn Asp Ser Val Glu Leu Ser
370 375 380
Gln Asn Glu Gln Lys Leu Ala Ala Trp Leu Ala Lys Arg Gly Pro Ile
385 390 395 400
Ser Val Ala Ile Asn Ala Phe Gly Met Gln Phe Tyr Arg His Gly Ile
405 410 415
Ser Arg Pro Leu Arg Pro Leu Cys Ser Pro Trp Leu Ile Asp His Ala
420 425 430
Val Leu Leu Val Gly Tyr Gly Asn Arg Ser Asp Val Pro Phe Trp Ala
435 440 445
Ile Lys Asn Ser Trp Gly Thr Asp Trp Gly Glu Lys Gly Tyr Tyr Tyr
450 455 460
Leu His Arg Gly Ser Gly Ala Cys Gly Val Asn Thr Met Ala Ser Ser
465 470 475 480
Ala Val Val Asp

<210> 382
<211> 2002
<212> DNA
<213> Homo sapiens

<400> 382
aattccgcgg caaccgctcc ggcaacgcca accgctccgc tgcgcgcagg ctgggctgca 60
ggctctcggc tgcagcgctg ggctggtgtg cagtggtgcg accacggctc acggcagcct 120
cagccaccca gatgtaagcg atctggttcc cacctcagcc ttccgagtag tggatctagg 180
atctggcttc caacatgtgg cagctctggg cctccctctg ctgcctgctg gtgttggcca 240
atgcccggag caggccctct ttccatcccg tgtcggatga gctggtcaac tatgtcaaca 300
aacggaatac cacgtggcag gccgggcaca acttctacaa cgtggacatg agctacttga 360
agaggctatg tggtaccttc ctgggtgggc ccaagccacc ccagagagtt atgtttaccg 420
aggacctgaa gctgcctgca agcttcgatg cacgggaaca atggccacag tgtcccacca 480
tcaaagagat cagagaccag ggctcctgtg gctcctgctg ggccttcggg gctgtggaag 540
ccatctctga ccgcatctgc atccacacca atgcgcacgt cagcgtggag gtgtcggcgg 600
aggacctgct cacctgctgt ggcagcatgt gtggggacgg ctgtaatggt ggctatcctg 660
ctgaagcttg gaacttctgg acaagaaaag gcctggtttc tggtggcctc tatgaatccc 720
atgtagggtg cagaccgtac tccatccctc cctgtgagca ccacgtcaac ggctcccggc 780
ccccatgcac gggggaggga gataccccca agtgtagcaa gatctgtgag cctggctaca 840
gcccgaccta caaacaggac aagcactacg gatacaattc ctacagcgtc tccaatagcg 900
agaaggacat catggccgag atctacaaaa acggccccgt ggagggagct ttctctgtgt 960
attcggactt cctgctctac aagtcaggag tgtaccaaca cgtcaccgga gagatgatgg 1020

```
gtggccatgc catccgcatc ctgggctggg gagtggagaa tggcacaccc tactggctgg 1080
ttgccaactc ctggaacact gactggggtg acaatggctt ctttaaaata ctcagaggac 1140
aggatcactg cggaatcgaa tcagaagtgg tggctggaat tccacgcacc gatcagtact 1200
gggaaaagat ctaatctgcc gtgggcctgt cgtgccagtc ctgggggcga gatcgggggta 1260
gaaagtcatt ttattcttta agttcacgta agatacaagt ttcaggcagg gtctgaagga 1320
ctggattggc caaagtcctc caaggagacc aagtcctggc tacatcccag cctgtggtta 1380
cagtgcagac aggccatgtg agccaccgct gccagcacag agcgtccttc cccctgtaga 1440
ctagtgccgt gggagtacct gctgcccagc tgctgtggcc ccctccgtga tccatccatc 1500
tccagggagc aagacagaga cgcaggatgg aaagcggagt tcctaacagg atgaaagttc 1560
ccccatcagt tcccccagta cctccaagca agtagctttc cacatttgtc acagaaatca 1620
gaggagagat ggtgttggga gcccctttgga gaacgccagt ctccaggtcc ccctgcatct 1680
atcgagtttg caatgtcaca acctctctga tcttgtgctc agcatgattc tttaatagaa 1740
gttttatttt tcgtgcactc tgctaatcat gtgggtgagc cagtggaaca gcgggagcct 1800
gtgctggttt gcagattgcc tcctaatgac gcggctcaaa aggaaaccaa gtggtcagga 1860
gttgtttctg acccactgat ctctactacc acaaggaaaa tagtttagga gaaaccagct 1920
tttactgttt ttgaaaaatt acagcttcac cctgtcaagt taacaaggaa tgcctgtgcc 1980
aataaaaggt ttctccaact tg                                          2002
```

<210> 383
<211> 339
<212> PRT
<213> Homo sapiens

<400> 383

```
Met Trp Gln Leu Trp Ala Ser Leu Cys Cys Leu Leu Val Leu Ala Asn
 1               5                  10                  15
Ala Arg Ser Arg Pro Ser Phe His Pro Leu Ser Asp Glu Leu Val Asn
            20                  25                  30
Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr
        35                  40                  45
Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly
    50                  55                  60
Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu
65                  70                  75                  80
Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile
                85                  90                  95
Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly
            100                 105                 110
Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His
        115                 120                 125
Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser
    130                 135                 140
Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn
145                 150                 155                 160
Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His
                165                 170                 175
Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn
            180                 185                 190
Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser
        195                 200                 205
Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His
    210                 215                 220
Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met
225                 230                 235                 240
Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr
                245                 250                 255
Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly
            260                 265                 270
```

```
Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu
        275                 280                 285
Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp
    290                 295                 300
Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly
305                 310                 315                 320
Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp
                325                 330                 335
Glu Lys Ile
```

<210> 384
<211> 1292
<212> DNA
<213> Carica papaya

<400> 384
atccattccc acttaagaag taaaaagata tagctagtgt cacaatggct atgatacctt 60
caatttcaaa gttgcttttt gttgcaatat gtctttttgt ttatatgggt ttgtcatttg 120
gtgatttttc tattgtgggt tattctcaaa atgacttgac atccactgaa agacttattc 180
agctatttga atcgtggatg ttgaagcaca ataagattta taagaatatt gatgaaaaaa 240
tctacagatt tgaaattttt aaagataatc ttaaatatat tgatgagaca aataagaaaa 300
ataacagtta ttggcttgga ttaaatgtgt ttgctgatat gagcaatgat gaattcaaag 360
aaaagtatac tggttctatt gctggaaatt atacaacaac cgaactatca tacgaagaag 420
tgcttaatga tggtgatgta aatatcccgg agtatgtcga ttggagacaa aaaggagctg 480
tcactcctgt aaaaaatcag ggttcttgtg gtagttgttg ggcattctca gctgttgtaa 540
ctatagaggg aataattaag attagaactg ggaacttaaa tgaatactca gagcaagaac 600
tgcttgactg cgacagacgt agctacgggt gcaatggagg ttacccttgg agtgcacttc 660
aattagtggc tcaatatggt attcactaca gaaatactta cccatatgag ggagtgcaac 720
gttattgtcg ctcaagggag aaaggtcctt atgcagccaa aaccgatggg gttcgacaag 780
tgcaaccata taatgaaggg gctctcttat attcaattgc aaaccaacct gtgagcgttg 840
tccttgaagc tgctggaaaa gatttccaat tatatagagg gggaatattt gtggggccat 900
gcggaaacaa agtagatcat gcagtcgcag cagttgggta tggaccaaat tacatactca 960
taaagaattc atggggtaca ggatggggtg aaaatggata tataagaatc aaaagaggca 1020
ctggaaactc ctatggagta tgtggacttt atacaagctc attctatcct gttaaaaact 1080
gatgagatca cggctttcat aaaatccctt atatatatat atatatatag aacttgtata 1140
ctcatcgtgt gttgaaataa taaatgagag gattaataat ttgtgtaatc ctatatatca 1200
cagtttgttg tgacaaactt ttgcatcgct tgttatatta tttgtaataa tgtttgtttt 1260
gattgaataa acttttacat atacttttat gc 1292

<210> 385
<211> 345
<212> PRT
<213> Carica papaya

<400> 385
```
Met Ala Met Ile Pro Ser Ile Ser Lys Leu Leu Phe Val Ala Ile Cys
 1               5                  10                  15
Leu Phe Val Tyr Met Gly Leu Ser Phe Gly Asp Phe Ser Ile Val Gly
            20                  25                  30
Tyr Ser Gln Asn Asp Leu Thr Ser Thr Glu Arg Leu Ile Gln Leu Phe
        35                  40                  45
Glu Ser Trp Met Leu Lys His Asn Lys Ile Tyr Lys Asn Ile Asp Glu
    50                  55                  60
Lys Ile Tyr Arg Phe Glu Ile Phe Lys Asp Asn Leu Lys Tyr Ile Asp
65                  70                  75                  80
Glu Thr Asn Lys Lys Asn Asn Ser Tyr Trp Leu Gly Leu Asn Val Phe
```

```
                85                  90                  95
Ala Asp Met Ser Asn Asp Glu Phe Lys Glu Lys Tyr Thr Gly Ser Ile
            100                 105                 110
Ala Gly Asn Tyr Thr Thr Thr Glu Leu Ser Tyr Glu Glu Val Leu Asn
        115                 120                 125
Asp Gly Asp Val Asn Ile Pro Glu Tyr Val Asp Trp Arg Gln Lys Gly
    130                 135                 140
Ala Val Thr Pro Val Lys Asn Gln Gly Ser Cys Gly Ser Cys Trp Ala
145                 150                 155                 160
Phe Ser Ala Val Val Thr Ile Glu Gly Ile Ile Lys Ile Arg Thr Gly
                165                 170                 175
Asn Leu Asn Glu Tyr Ser Glu Gln Glu Leu Leu Asp Cys Asp Arg Arg
            180                 185                 190
Ser Tyr Gly Cys Asn Gly Gly Tyr Pro Trp Ser Ala Leu Gln Leu Val
        195                 200                 205
Ala Gln Tyr Gly Ile His Tyr Arg Asn Thr Tyr Pro Tyr Glu Gly Val
    210                 215                 220
Gln Arg Tyr Cys Arg Ser Arg Glu Lys Gly Pro Tyr Ala Ala Lys Thr
225                 230                 235                 240
Asp Gly Val Arg Gln Val Gln Pro Tyr Asn Glu Gly Ala Leu Leu Tyr
                245                 250                 255
Ser Ile Ala Asn Gln Pro Val Ser Val Val Leu Glu Ala Ala Gly Lys
            260                 265                 270
Asp Phe Gln Leu Tyr Arg Gly Gly Ile Phe Val Gly Pro Cys Gly Asn
        275                 280                 285
Lys Val Asp His Ala Val Ala Ala Val Gly Tyr Gly Pro Asn Tyr Ile
    290                 295                 300
Leu Ile Lys Asn Ser Trp Gly Thr Gly Trp Gly Glu Asn Gly Tyr Ile
305                 310                 315                 320
Arg Ile Lys Arg Gly Thr Gly Asn Ser Tyr Gly Val Cys Gly Leu Tyr
                325                 330                 335
Thr Ser Ser Phe Tyr Pro Val Lys Asn
            340                 345
```

<210> 386
<211> 1845
<212> DNA
<213> Trypanosoma cruzi

<400> 386

```
atgtctggct gggcgcgtgc gctgttgctc gcggccgtcc tggtcgtcat ggcgtgcctc 60
gtccccgcgg cgacggcgag cctgcatgcg gaggagacgc tgacgtcgca attcgcagaa 120
ttcaagcaga agcatggcag ggtgtacgag agcgccgcgg aggaggcgtt ccgcctgagc 180
gtgttcaggg agaacctgtt tcttgcgagg ctgcacgccg cggcaaaccc acacgcgacc 240
ttcggcgtca cgcccttctc ggacctcacg cgcgaggaat tccggtcccg ctaccacaac 300
ggcgcggcgc actttgcggc ggcgcaggag cgcgcgagag tgccggtgaa ggtggaggta 360
gttggcgcgc ccgcggcagt ggattggcgt gcgagaggcg ccgtgacagc cgtcaaggac 420
cagggccaat gcggttcgtg ctgggccttc tccgccattg gcaacgttga gtgccagtgg 480
tttcttgccg gccacccgct gacgaacctg tcggagcaga tgctcgtgtc gtgcgacaaa 540
acggactctg gctgcagtgg tggcctgatg aacaacgcct ttgagtggat tgtgcaggag 600
aataacggcg ccgtgtacac ggaggacagc tacccttatg cgtcgggcga ggggatatcg 660
ccgccgtgca cgacgtcagg ccacacggtg ggtgccacga ttaccggtca cgttgaatta 720
cctcaggacg aggcccaaat agccgcatgg cttgcagtca atggcccggt tgccgttgcc 780
gtcgacgcca gcagctggat gacctacacg ggcggcgtta tgacgagctg cgtctccgag 840
cagctggatc acggcgttct tctcgtcggc tacaatgaca gcgccgcagt gccgtactgg 900
atcatcaaga actcgtggac cacgcagtgg ggcgaggaag gctacatccg cattgcaaag 960
ggctcgaacc agtgccttgt caaggaggag gcgagctccg cggtggtcgg tggtcccgga 1020
```

```
cccactcccg agccaaccac cacgacaacc acaagtgccc caggaccgtc cccatcgtac 1080
tttgtgcaga tgtcctgcac tgacgctgcg tgcattgtcg ggtgcgagaa cgtgacgtta 1140
ccgaccggtc agtgtctcct gaccaccagc ggcgtctctg ccattgtcac gtgcggtgct 1200
gagactctca cagaagaagt cttccttacg agtacgcact gcagcggccc atcggtgagg 1260
tcctctgttc ctctcaacaa atgcaaccgg cttttaagag gctccgttga gttcttctgc 1320
ggctccagct ccagtggccg actggccgac gtggacaggc agcgtcgcca tcagccatac 1380
cacagccgtc atcgccgcct ctgagggcac tctttgtttc tgatgctgcc ttttctctca 1440
ttttactttt ttattattat tgagcgagcg tcggtgctgc ggcacactgg gcaaataagt 1500
cccagtggag tggattgttt attgatttgc tccatgtatg tgttttcttt tttgtgcaca 1560
actgcaaata tgtgtccgcg atcgacgtct cagccacgcg tgtgtttttt ctattatatg 1620
cttctgttga gcgcccgagc attccccact gtggctgaac ccaccgccgt ccccgactgt 1680
cacccgacca tgcggggcgg ggtggcgtgg caacgctcct ttgccgcggc gtgcacatac 1740
acgcgcgcat gcttcttctc tccacgtcaa cgccgacacc accacagtct gaaggtgacg 1800
ctgttgaagg cacacaagga aggaaacaca cccacacaag cagta                 1845

<210> 387
<211> 467
<212> PRT
<213> Trypanosoma cruzi

<400> 387
Met Ser Gly Trp Ala Arg Ala Leu Leu Leu Ala Ala Val Leu Val Val
 1               5                  10                  15
Met Ala Cys Leu Val Pro Ala Ala Thr Ala Ser Leu His Ala Glu Glu
            20                  25                  30
Thr Leu Thr Ser Gln Phe Ala Glu Phe Lys Gln Lys His Gly Arg Val
        35                  40                  45
Tyr Glu Ser Ala Ala Glu Glu Ala Phe Arg Leu Ser Val Phe Arg Glu
    50                  55                  60
Asn Leu Phe Leu Ala Arg Leu His Ala Ala Ala Asn Pro His Ala Thr
65                  70                  75                  80
Phe Gly Val Thr Pro Phe Ser Asp Leu Thr Arg Glu Glu Phe Arg Ser
                85                  90                  95
Arg Tyr His Asn Gly Ala Ala His Phe Ala Ala Ala Gln Glu Arg Ala
            100                 105                 110
Arg Val Pro Val Lys Val Glu Val Val Gly Ala Pro Ala Ala Val Asp
        115                 120                 125
Trp Arg Ala Arg Gly Ala Val Thr Ala Val Lys Asp Gln Gly Gln Cys
    130                 135                 140
Gly Ser Cys Trp Ala Phe Ser Ala Ile Gly Asn Val Glu Cys Gln Trp
145                 150                 155                 160
Phe Leu Ala Gly His Pro Leu Thr Asn Leu Ser Glu Gln Met Leu Val
                165                 170                 175
Ser Cys Asp Lys Thr Asp Ser Gly Cys Ser Gly Gly Leu Met Asn Asn
            180                 185                 190
Ala Phe Glu Trp Ile Val Gln Glu Asn Asn Gly Ala Val Tyr Thr Glu
        195                 200                 205
Asp Ser Tyr Pro Tyr Ala Ser Gly Glu Gly Ile Ser Pro Pro Cys Thr
    210                 215                 220
Thr Ser Gly His Thr Val Gly Ala Thr Ile Thr Gly His Val Glu Leu
225                 230                 235                 240
Pro Gln Asp Glu Ala Gln Ile Ala Ala Trp Leu Ala Val Asn Gly Pro
                245                 250                 255
Val Ala Val Ala Val Asp Ala Ser Ser Trp Met Thr Tyr Thr Gly Gly
            260                 265                 270
Val Met Thr Ser Cys Val Ser Glu Gln Leu Asp His Gly Val Leu Leu
        275                 280                 285
Val Gly Tyr Asn Asp Ser Ala Ala Val Pro Tyr Trp Ile Ile Lys Asn
```

```
    290                 295                 300
Ser Trp Thr Thr Gln Trp Gly Glu Glu Gly Tyr Ile Arg Ile Ala Lys
305                 310                 315                 320
Gly Ser Asn Gln Cys Leu Val Lys Glu Glu Ala Ser Ser Ala Val Val
                325                 330                 335
Gly Gly Pro Gly Pro Thr Pro Glu Pro Thr Thr Thr Thr Thr Thr Ser
            340                 345                 350
Ala Pro Gly Pro Ser Pro Ser Tyr Phe Val Gln Met Ser Cys Thr Asp
        355                 360                 365
Ala Ala Cys Ile Val Gly Cys Glu Asn Val Thr Leu Pro Thr Gly Gln
    370                 375                 380
Cys Leu Leu Thr Thr Ser Gly Val Ser Ala Ile Val Thr Cys Gly Ala
385                 390                 395                 400
Glu Thr Leu Thr Glu Glu Val Phe Leu Thr Ser Thr His Cys Ser Gly
                405                 410                 415
Pro Ser Val Arg Ser Ser Val Pro Leu Asn Lys Cys Asn Arg Leu Leu
            420                 425                 430
Arg Gly Ser Val Glu Phe Phe Cys Gly Ser Ser Ser Ser Gly Arg Leu
        435                 440                 445
Ala Asp Val Asp Arg Gln Arg Arg His Gln Pro Tyr His Ser Arg His
    450                 455                 460
Arg Arg Leu
465
```

<210> 388
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 388
Leu Pro Ser Arg
 1

<210> 389
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 389
Ser Leu Leu Arg
 1

<210> 390
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 390
His Arg Gly Arg
1

<210> 391
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 391
Gly Ala Thr Arg
1

<210> 392
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 392
Ser Leu Gly Arg
1

<210> 393
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 393
Val Phe Ala Lys
1

<210> 394
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 394
Arg Glu Phe Lys
1

<210> 395
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 395
Gly Leu Ala Arg
1

<210> 396
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 396
Arg Leu Gly Arg
1

<210> 397
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 397
Ala Glu Gly Lys
1

<210> 398
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 398
Gln His Ala Arg
1

<210> 399
<211> 4
<212> PRT
<213> Artificial Sequence

<220>

<223> Protease cleavage site

<400> 399
Leu Gly Leu Ala
1

<210> 400
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 400
Leu Ser Val Val
1

<210> 401
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 401
Arg Gln Ala Arg
1

<210> 402
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 402
Pro Arg Phe Lys
1

<210> 403
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Protease cleavage site

<400> 403
Lys Gln Gly Arg
1

<210> 404
<211> 855
<212> PRT
<213> Homo sapiens

<400> 404
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 405
<211> 855
<212> PRT
<213> Homo sapiens

<400> 405

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

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                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Val Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 406
<211> 855
<212> PRT
<213> Homo sapiens

<400> 406
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Asp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 407
<211> 855
<212> PRT
<213> Homo sapiens

<400> 407
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Glu Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 408
<211> 855
<212> PRT
<213> Homo sapiens

<400> 408
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Ala Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 409
<211> 855
<212> PRT
<213> Homo sapiens

<400> 409
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                    405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 410
<211> 855
<212> PRT
<213> Homo sapiens

<400> 410
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asn Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 411
<211> 855
<212> PRT
<213> Homo sapiens

<400> 411
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 412
<211> 855
<212> PRT
<213> Homo sapiens

<400> 412
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 413
<211> 855
<212> PRT
<213> Homo sapiens

<400> 413
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Ala Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 414
<211> 855
<212> PRT
<213> Homo sapiens

<400> 414

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Trp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 415
<211> 855
<212> PRT
<213> Homo sapiens

<400> 415

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Arg Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 416
<211> 855
<212> PRT
<213> Homo sapiens

<400> 416

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Arg Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Arg Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 417
<211> 855
<212> PRT
<213> Homo sapiens

<400> 417
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Arg Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Arg Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Ala Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 418
<211> 855
<212> PRT
<213> Homo sapiens

<400> 418
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Trp Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Arg Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Arg Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 419
<211> 855
<212> PRT
<213> Homo sapiens

<400> 419
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro His Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 420
<211> 855
<212> PRT
<213> Homo sapiens

<400> 420
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Gln Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 421
<211> 855
<212> PRT
<213> Homo sapiens

<400> 421
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asn Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 422
<211> 855
<212> PRT
<213> Homo sapiens

<400> 422

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly His Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 423
<211> 855
<212> PRT
<213> Homo sapiens

<400> 423
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Ala Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 424
<211> 855
<212> PRT
<213> Homo sapiens

<400> 424

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Val Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 425
<211> 855
<212> PRT
<213> Homo sapiens

<400> 425

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Phe Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 426
<211> 855
<212> PRT
<213> Homo sapiens

<400> 426
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Ser Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 427
<211> 855
<212> PRT
<213> Homo sapiens

<400> 427
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Thr Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 428
<211> 855
<212> PRT
<213> Homo sapiens

<400> 428

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Leu Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 429
<211> 855
<212> PRT
<213> Homo sapiens

<400> 429

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Ile Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 430
<211> 855
<212> PRT
<213> Homo sapiens

<400> 430

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Phe Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 431
<211> 855
<212> PRT
<213> Homo sapiens

<400> 431
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Phe Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 432
<211> 855
<212> PRT
<213> Homo sapiens

<400> 432
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

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                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Ala Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 433
<211> 855
<212> PRT
<213> Homo sapiens

<400> 433
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Val Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 434
<211> 855
<212> PRT
<213> Homo sapiens

<400> 434
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Ser Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 435
<211> 855
<212> PRT
<213> Homo sapiens

<400> 435

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Gly Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 436
<211> 855
<212> PRT
<213> Homo sapiens

<400> 436
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Phe Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 437
<211> 855
<212> PRT
<213> Homo sapiens

<400> 437
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Tyr Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 438
<211> 855
<212> PRT
<213> Homo sapiens

<400> 438

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Ala Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 439
<211> 855
<212> PRT
<213> Homo sapiens

<400> 439

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Val Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 440
<211> 855
<212> PRT
<213> Homo sapiens

<400> 440
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Phe Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 441
<211> 855
<212> PRT
<213> Homo sapiens

<400> 441
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1   5   10   15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20   25   30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35   40   45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50   55   60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65   70   75   80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85   90   95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100   105   110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115   120   125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130   135   140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145   150   155   160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165   170   175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180   185   190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195   200   205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210   215   220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225   230   235   240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245   250   255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260   265   270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275   280   285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290   295   300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305   310   315   320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325   330   335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340   345   350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355   360   365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370   375   380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385   390   395   400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Arg Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 442
<211> 855
<212> PRT
<213> Homo sapiens

<400> 442
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Lys Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 443
<211> 855
<212> PRT
<213> Homo sapiens

<400> 443

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
```

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Ala Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 444
<211> 855
<212> PRT
<213> Homo sapiens

<400> 444
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1   5   10   15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20   25   30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35   40   45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50   55   60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65   70   75   80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85   90   95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100   105   110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115   120   125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130   135   140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145   150   155   160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165   170   175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180   185   190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195   200   205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210   215   220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225   230   235   240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245   250   255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260   265   270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275   280   285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290   295   300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305   310   315   320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325   330   335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340   345   350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355   360   365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370   375   380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385   390   395   400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Val Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 445
<211> 855
<212> PRT
<213> Homo sapiens

<400> 445
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Glu Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 446
<211> 855
<212> PRT
<213> Homo sapiens

<400> 446
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Trp Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 447
<211> 855
<212> PRT
<213> Homo sapiens

<400> 447
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Tyr Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 448
<211> 855
<212> PRT
<213> Homo Sapiens

<220>
<221> VARIANT
<222> 381
<223> Ser

<220>
<221> VARIANT
<222> 674
<223> Val

<400> 448
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg

```
                    325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
                340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
            355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
```

785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 449
<211> 855
<212> PRT
<213> Mus musculus

<400> 449
Met Gly Ser Asn Arg Gly Arg Lys Ala Gly Gly Gly Ser Gln Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg Leu Glu Asn Met Asn Gly Phe
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Ala Asn Asn Ala Lys Lys Val Glu
35 40 45
Lys Arg Gly Pro Arg Arg Trp Val Val Leu Val Ala Val Leu Phe Ser
50 55 60
Phe Leu Leu Leu Ser Leu Met Ala Gly Leu Leu Val Trp His Phe His
65 70 75 80
Tyr Arg Asn Val Arg Val Gln Lys Val Phe Asn Gly His Leu Arg Ile
85 90 95
Thr Asn Glu Ile Phe Leu Asp Ala Tyr Glu Asn Ser Thr Ser Thr Glu
100 105 110
Phe Ile Ser Leu Ala Ser Gln Val Lys Glu Ala Leu Lys Leu Leu Tyr
115 120 125
Asn Glu Val Pro Val Leu Gly Pro Tyr His Lys Lys Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Pro His Leu Ala Glu Glu Val Asp Arg Ala Met Ala Val Glu
165 170 175
Arg Val Val Thr Leu Pro Pro Arg Ala Arg Ala Leu Lys Ser Phe Val
180 185 190
Leu Thr Ser Val Val Ala Phe Pro Ile Asp Pro Arg Met Leu Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Ala Leu His Ala His Gly Ala Ala
210 215 220
Val Thr Arg Phe Thr Thr Pro Gly Phe Pro Asn Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Val Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Val Ala Pro Cys Asp Glu His Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asp Ser Leu Ser Pro Met Glu Pro His
275 280 285
Ala Val Val Arg Leu Cys Gly Thr Phe Ser Pro Ser Tyr Asn Leu Thr
290 295 300
Phe Leu Ser Ser Gln Asn Val Phe Leu Val Thr Leu Ile Thr Asn Thr
305 310 315 320
Asp Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Lys

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                    325                 330                 335
Met Ser Ser Cys Gly Gly Phe Leu Ser Asp Thr Gln Gly Thr Phe Ser
                340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asn Cys Thr Trp
            355                 360                 365
Asn Ile Lys Val Pro Asn Asn Arg Asn Val Lys Val Arg Phe Lys Leu
    370                 375                 380
Phe Tyr Leu Val Asp Pro Asn Val Pro Val Gly Ser Cys Thr Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Ser Ser Asn Ser Ser Lys Ile Thr Val His Phe His Ser Asp
            420                 425                 430
His Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Asn Asp Pro Cys Pro Gly Met Phe Met Cys Lys Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Pro Asp Tyr
465                 470                 475                 480
Ser Asp Glu Arg Tyr Cys Arg Cys Asn Ala Thr His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Gln Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Gly Ser Asp Glu Glu Gly Cys Ser Cys Pro Ala Gly
        515                 520                 525
Ser Phe Lys Cys Ser Asn Gly Lys Cys Leu Pro Gln Ser Gln Lys Cys
    530                 535                 540
Asn Gly Lys Asp Asn Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Asp
545                 550                 555                 560
Ser Val Asn Val Val Ser Cys Thr Lys Tyr Thr Tyr Arg Cys Gln Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Thr Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asn Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Lys Gln Ala Arg Val Val Gly Gly Thr Asn Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Leu
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asp Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Phe Gln Asp Asp Lys Asn Phe Lys Tyr Ser Asp Tyr Thr Met Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu Leu Asp Gln Ser Lys Arg Ser Ala Ser Gly
        675                 680                 685
Val Gln Glu Leu Lys Leu Lys Arg Ile Ile Thr His Pro Ser Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Ser
705                 710                 715                 720
Val Glu Tyr Ser Thr Val Val Arg Pro Ile Cys Leu Pro Asp Ala Thr
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Lys Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asp Leu Met Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
```

785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Ala Glu Lys Asp Gly
805 810 815
Arg Met Phe Gln Ala Gly Val Val Ser Trp Gly Glu Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Val Val Arg Asp Trp
835 840 845
Ile Lys Glu His Thr Gly Val
850 855

<210> 450
<211> 855
<212> PRT
<213> Rattus norvegicus

<400> 450
Met Gly Asn Asn Arg Gly Arg Lys Ala Gly Gly Gly Ser Gln Asp Phe
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Gly Ala Gly Leu Lys Tyr Asn Ser Arg Leu Glu Asn Met Asn Gly Phe
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Ala Lys Gln Val Glu
35 40 45
Lys Arg Gly Pro Arg Arg Trp Val Val Met Val Ala Val Val Phe Ser
50 55 60
Phe Leu Leu Leu Ser Leu Met Ala Gly Leu Leu Val Trp His Phe His
65 70 75 80
Tyr Arg Asn Val Arg Ile Gln Lys Val Phe Asn Gly His Leu Arg Ile
85 90 95
Thr Asn Glu Asn Phe Leu Asp Ala Tyr Glu Asn Ser Thr Ser Thr Glu
100 105 110
Phe Ile Ser Leu Ala Ser Gln Val Lys Glu Ala Leu Lys Leu Met Tyr
115 120 125
Ser Glu Val Pro Val Leu Gly Pro Tyr His Lys Lys Ser Thr Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Pro His Leu Glu Glu Glu Val Asp Arg Ala Met Ala Val Glu
165 170 175
Arg Val Val Thr Leu Pro Pro Arg Ala Arg Ala Leu Lys Ser Phe Val
180 185 190
Leu Thr Ser Val Val Ala Phe Pro Ile Asp Pro Arg Met Leu Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Ala Leu His Ala Arg Gly Arg Thr
210 215 220
Val Thr Arg Phe Thr Thr Pro Gly Phe Pro Asn Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Val Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Val Ala Pro Cys Asp Gly His Asp
260 265 270
Ser Asp Leu Val Thr Val Tyr Asp Ser Leu Ser Pro Met Glu Pro His
275 280 285
Ala Val Val Arg Leu Cys Gly Thr Phe Ser Pro Ser Tyr Asn Leu Thr
290 295 300
Phe Leu Ser Ser Gln Asn Val Phe Leu Val Thr Leu Ile Thr Asn Thr
305 310 315 320
Asp Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Lys

```
                    325                 330                 335
Met Ser Ser Cys Gly Gly Leu Leu Ser Glu Ala Gln Gly Thr Phe Ser
                340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asn Cys Thr Trp
            355                 360                 365
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Tyr Val Glu Ile Asn Gly Glu Lys Phe Cys Gly Glu Arg Ser Gln Phe
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Val Val Ser Ser Asn Ser Ser Lys Ile Thr Val His Phe His Ser Asp
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His Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
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Ile Arg Lys Asp Leu Arg Cys Asp Gly Trp Ala Asp Cys Pro Asp Tyr
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Ser Asp Glu Arg His Cys Arg Cys Asn Ala Thr His Gln Phe Met Cys
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Lys Asn Gln Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
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Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Thr Val Val Arg Pro Ile Cys Leu Pro Asp Asn Thr
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His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
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Thr Lys Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
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gcggagtccc attcctgggc ccctaccaca aggagtcggc tgtgacggcc ttcagcgagg 480
gcagcgtcat cgcctactac tggtctgagt tcagcatccc gcagcacctg gtggaggagg 540
ccgagcgcgt catggccgag gagcgcgtag tcatgctgcc cccgcgggcg cgctccctga 600
agtcctttgt ggtcacctca gtggtggctt tccccacgga ctccaaaaca gtacagagga 660
cccaggacaa cagctgcagc tttggcctgc acgcccgcgg tgtggagctg atgcgcttca 720
ccacgcccgg cttccctgac agcccctacc ccgctcatgc ccgctgccag tgggccctgc 780
gggggacgc cgactcagtg ctgagcctca ccttccgcag ctttgacctt gcgtcctgcg 840
acgagcgcgg cagcgacctg gtgacggtgt acaacaccct gagccccatg gagccccacg 900
ccctggtgca gttgtgtggc acctaccctc cctcctacaa cctgaccttc cactcctccc 960
agaacgtcct gctcatcaca ctgataacca acactgagcg gcggcatccc ggctttgagg 1020
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acgccggcca ccagttcacg tgcaagaaca agttctgcaa gcccctcttc tgggtctgcg 1560
acagtgtgaa cgactgcgga gacaacagcg acgagcaggg gtgcagttgt ccggcccaga 1620
ccttcaggtg ttccaatggg aagtgcctct cgaaaagcca gcagtgcaat gggaaggacg 1680
actgtgggga cgggtccgac gaggcctcct gccccaaggt gaacgtcgtc acttgtacca 1740
aacacaccta ccgctgcctc aatgggctct gcttgagcaa gggcaaccct gagtgtgacg 1800
ggaaggagga ctgtagcgac ggctcagatg agaaggactg cgactgtggg ctgcggtcat 1860
tcacgagaca ggctcgtgtt gttgggggca cggatgcgga tgagggcgag tggccctggc 1920
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gctggggaca cacccagtat ggaggcactg gcgcgctgat cctgcaaaag ggtgagatcc 2340
gcgtcatcaa ccagaccacc tgcgagaacc tcctgccgca gcagatcacg ccgcgcatga 2400
tgtgcgtggg cttcctcagc ggcggcgtgg actcctgcca gggtgattcc gggggacccc 2460
tgtccagcgt ggaggcggat gggcggatct tccaggccgg tgtggtgagc tggggagacg 2520
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tcaaagagaa cactggggta tagggccggg ggccacccaa atgtgtacac ctgcggggcc 2640
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agcgccccca gaacatacac tgtgaactca atctccaggg ctccaaatct gcctagaaaa 2760
cctctcgctt cctcagcctc caaagtggag ctgggaggta gaaggggagg acactggtgg 2820
ttctactgac ccaactgggg gcaaaggttt gaagacacag cctcccccgc cagccccaag 2880

ctgggccgag gcgcgtttgt gtatatctgc ctcccctgtc tgtaaggagc agcgggaacg 2940
gagcttcgga gcctcctcag tgaaggtggt ggggctgccg gatctgggct gtggggccct 3000
tgggccacgc tcttgaggaa gcccaggctc ggaggaccct ggaaaacaga cgggtctgag 3060
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aacattttat ttctttttaa aaaaaaaaa 3149

<210> 524
<211> 241
<212> PRT
<213> Homo sapiens

<400> 524
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Leu Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 525
<211> 241
<212> PRT
<213> Homo sapiens

<400> 525
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60

```
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Tyr Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
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<210> 526
<211> 241
<212> PRT
<213> Homo sapiens

<400> 526

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Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Glu Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
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Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 527
<211> 241
<212> PRT
<213> Homo sapiens

<400> 527
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Lys Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 528
<211> 241
<212> PRT
<213> Homo sapiens

<400> 528
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu

65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Tyr Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 529
<211> 855
<212> PRT
<213> Homo sapiens

<400> 529
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala

225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn

```
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Leu Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 530
<211> 855
<212> PRT
<213> Homo sapiens

<400> 530

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
```

```
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
```

```
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Tyr Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855

<210> 531
<211> 855
<212> PRT
<213> Homo sapiens

<400> 531
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                   5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
```

```
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
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705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Glu Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
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Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 532
<211> 855
<212> PRT
<213> Homo sapiens

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Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255

Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720

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Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Lys Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855

<210> 533
<211> 855
<212> PRT
<213> Homo sapiens

<400> 533
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 1                5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
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                260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
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                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Tyr Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 534
<211> 723
<212> DNA
<213> Homo sapiens

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gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
ttcctgggct tgcacgacca gagccagcgc agcgcccctg gggtgcagga gcgcaggctc 240
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gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gttgcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
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gta 723

<210> 535
<211> 723
<212> DNA
<213> Homo sapiens

<400> 535
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gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
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ctggagctgg agaaaccggc agagtacagc tccatggtgc ggcccatctg cctgccggac 360
gcctcccatg tcttccctgc cggcaaggcc atctgggtca cgggctgggg acacacccag 420
tatggaggca ctggcgcgct gatcctgcaa aagggtgaga tccgcgtcat caaccagacc 480
acctgcgaga acctcctgcc gtatcagatc acgccgcgca tgatgtgcgt gggcttcctc 540
agcggcggcg tggactcctg ccagggtgat tccgggggac ccctgtccag cgtggaggcg 600
gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
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gta 723

<210> 536
<211> 723
<212> DNA
<213> Homo sapiens

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gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
aagccaggcg tgtacacaag gctccctctg tttcgggact ggatcaaaga gaacactggg 720
gta 723

<210> 537
<211> 723
<212> DNA
<213> Homo sapiens

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gatgggcgga tcttccaggc cggtgtggtg agctggggag acggctgcgc tcagaggaac 660
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gta 723

<210> 538
<211> 723
<212> DNA
<213> Homo sapiens

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gcacactgct acatcgatga cagaggattc aggtactcag accccacgca gtggacggcc 180
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gta

723

<210> 539
<211> 3149
<212> DNA
<213> Homo sapiens

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tcttcaatgg ctacatgagg atcacaaatg agaattttgt ggatgcctac gagaactcca 360
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<211> 124
<212> PRT
<213> Unknown

<220>
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            20   25   30
Thr Ala Leu Leu Asp Ser Gly Ala Asp Ile Thr Ile Ile Ser Glu Glu
        35   40   45
Asp Trp Pro Thr Asp Trp Pro Val Met Glu Ala Ala Asn Pro Gln Ile
    50   55   60
His Gly Ile Gly Gly Gly Ile Pro Met Arg Lys Ser Arg Asp Met Ile
65   70   75   80

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                85                  90                  95
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<212> DNA
<213> Homo sapiens

<400> 546

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<212> PRT
<213> Homo sapiens

<400> 547

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Leu Val Gln Lys Tyr Leu Glu Asn Tyr Tyr Asp Leu Lys Lys Asp Val
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Val Gly His Phe Arg Thr Phe Pro Gly Ile Pro Lys Trp Arg Lys Thr
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His Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp Leu Pro Lys Asp
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Thr Pro Leu Thr Phe Ser Arg Leu Tyr Glu Gly Glu Ala Asp Ile Met
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Ile Ser Phe Ala Val Arg Glu His Gly Asp Phe Tyr Pro Phe Asp Gly
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Pro Gly Asn Val Leu Ala His Ala Tyr Ala Pro Gly Pro Gly Ile Asn
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<212> DNA
<213> Homo sapiens

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<212> PRT
<213> Homo sapiens

<400> 549

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Gln Val Ser Tyr Val Ile Gln Ala Glu Gly Lys Glu His Ile Ile His
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Leu Glu Arg Asn Lys Asp Leu Leu Pro Glu Asp Phe Val Val Tyr Thr
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Tyr Asn Lys Glu Gly Thr Leu Ile Thr Asp His Pro Asn Ile Gln Asn
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His Cys His Tyr Arg Gly Tyr Val Glu Gly Val His Asn Ser Ser Ile
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Ser Lys Gly Asp Arg Phe Gly Asn Cys Gly Phe Ser Gly Asn Glu Tyr
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Ala Gly Lys Ile Cys Arg Asn Phe Gln Cys Val Asp Ala Ser Val Leu
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660 665 670
Cys Glu Thr Lys Gly Tyr Gly Gly Ser Val Asp Ser Gly Pro Thr Tyr
675 680 685
Asn Glu Met Asn Thr Ala Leu Arg Asp Gly Leu Leu Val Phe Phe Phe
690 695 700
Leu Ile Val Pro Leu Ile Val Cys Ala Ile Phe Ile Phe Ile Lys Arg
705 710 715 720
Asp Gln Leu Trp Arg Ser Tyr Phe Arg Lys Lys Arg Ser Gln Thr Tyr
725 730 735
Glu Ser Asp Gly Lys Asn Gln Ala Asn Pro Ser Arg Gln Pro Gly Ser
740 745 750

Val Pro Arg His Val Ser Pro Val Thr Pro Pro Arg Glu Val Pro Ile
755 760 765
Tyr Ala Asn Arg Phe Ala Val Pro Thr Tyr Ala Ala Lys Gln Pro Gln
770 775 780
Gln Phe Pro Ser Arg Pro Pro Pro Pro Gln Pro Lys Val Ser Ser Gln
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<212> DNA
<213> Homo sapiens

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gccaatgtac ataccttgtt atatgcagac atgtatttct tacgtacact gtacttctgt 3180
gtgcaattgt aaacagaaat tgcaatatgg atgtttcttt gtattataaa atttttccgc 3240
tcttaattaa aaattactgt ttaattgaca tactcaggat aacagagaat ggtggtattc 3300
agtggtccag gattctgtaa tgctttacac aggcagtttt gaaatgaaaa tcaatttacc 3360
tttctgttac gatggagttg gttttgatac tcatttttc tttatcacat ggctgctacg 3420
ggcacaagtg actatactga agaacacagt taagtgttgt gcaaactgga catagcagca 3480
catactactt cagagttcat gatgtagatg tctggtttct gcttacgtct tttaaacttt 3540
ctaattcaat tccatttttc aattaatagg tgaaatttta ttcatgcttt gatagaaatt 3600
atgtcaatga aatgattctt tttatttgta gcctacttat ttgtgttttt catatatctg 3660
aaatatgcta attatgtttt ctgtctgata tggaaaagaa aagctgtgtc tttatcaaaa 3720
tatttaaacg gttttttcag catatcatca ctgatcattg gtaaccacta aagatgagta 3780
atttgcttaa gtagtagtta aaattgtaga taggccttct gacatttttt ttcctaaaat 3840
ttttaacagc attgaaggtg aaacagcaca atgtcccatt ccaaatttat ttttgaaaca 3900
gatgtaaata attggcattt taaagag                                     3927
```

<210> 551
<211> 748
<212> PRT
<213> Homo sapiens

<400> 551

```
Met Val Leu Leu Arg Val Leu Ile Leu Leu Leu Ser Trp Ala Ala Gly
 1               5                  10                  15
Met Gly Gly Gln Tyr Gly Asn Pro Leu Asn Lys Tyr Ile Arg His Tyr
            20                  25                  30
Glu Gly Leu Ser Tyr Asn Val Asp Ser Leu His Gln Lys His Gln Arg
        35                  40                  45
Ala Lys Arg Ala Val Ser His Glu Asp Gln Phe Leu Arg Leu Asp Phe
    50                  55                  60
His Ala His Gly Arg His Phe Asn Leu Arg Met Lys Arg Asp Thr Ser
65                  70                  75                  80
Leu Phe Ser Asp Glu Phe Lys Val Glu Thr Ser Asn Lys Val Leu Asp
                85                  90                  95
Tyr Asp Thr Ser His Ile Tyr Thr Gly His Ile Tyr Gly Glu Glu Gly
            100                 105                 110
Ser Phe Ser His Gly Ser Val Ile Asp Gly Arg Phe Glu Gly Phe Ile
        115                 120                 125
Gln Thr Arg Gly Gly Thr Phe Tyr Val Glu Pro Ala Glu Arg Tyr Ile
    130                 135                 140
Lys Asp Arg Thr Leu Pro Phe His Ser Val Ile Tyr His Glu Asp Asp
145                 150                 155                 160
Ile Asn Tyr Pro His Lys Tyr Gly Pro Gln Gly Gly Cys Ala Asp His
                165                 170                 175
Ser Val Phe Glu Arg Met Arg Lys Tyr Gln Met Thr Gly Val Glu Glu
            180                 185                 190
Val Thr Gln Ile Pro Gln Glu Glu His Ala Ala Asn Gly Pro Glu Leu
```

```
        195                 200                 205
Leu Arg Lys Lys Arg Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln Leu
    210                 215                 220
Tyr Ile Gln Thr Asp His Leu Phe Phe Lys Tyr Tyr Gly Thr Arg Glu
225                 230                 235                 240
Ala Val Ile Ala Gln Ile Ser Ser His Val Lys Ala Ile Asp Thr Ile
                245                 250                 255
Tyr Gln Thr Thr Asp Phe Ser Gly Ile Arg Asn Ile Ser Phe Met Val
            260                 265                 270
Lys Arg Ile Arg Ile Asn Thr Thr Ala Asp Glu Lys Asp Pro Thr Asn
        275                 280                 285
Pro Phe Arg Phe Pro Asn Ile Gly Val Glu Lys Phe Leu Glu Leu Asn
    290                 295                 300
Ser Glu Gln Asn His Asp Asp Tyr Cys Leu Ala Tyr Val Phe Thr Asp
305                 310                 315                 320
Arg Asp Phe Asp Asp Gly Val Leu Gly Leu Ala Trp Val Gly Ala Pro
                325                 330                 335
Ser Gly Ser Ser Gly Gly Ile Cys Glu Lys Ser Lys Leu Tyr Ser Asp
            340                 345                 350
Gly Lys Lys Lys Ser Leu Asn Thr Gly Ile Ile Thr Val Gln Asn Tyr
        355                 360                 365
Gly Ser His Val Pro Pro Lys Val Ser His Ile Thr Phe Ala His Glu
    370                 375                 380
Val Gly His Asn Phe Gly Ser Pro His Asp Ser Gly Thr Glu Cys Thr
385                 390                 395                 400
Pro Gly Glu Ser Lys Asn Leu Gly Gln Lys Glu Asn Gly Asn Tyr Ile
                405                 410                 415
Met Tyr Ala Arg Ala Thr Ser Gly Asp Lys Leu Asn Asn Asn Lys Phe
            420                 425                 430
Ser Leu Cys Ser Ile Arg Asn Ile Ser Gln Val Leu Glu Lys Lys Arg
        435                 440                 445
Asn Asn Cys Phe Val Glu Ser Gly Gln Pro Ile Cys Gly Asn Gly Met
    450                 455                 460
Val Glu Gln Gly Glu Glu Cys Asp Cys Gly Tyr Ser Asp Gln Cys Lys
465                 470                 475                 480
Asp Glu Cys Cys Phe Asp Ala Asn Gln Pro Glu Gly Arg Lys Cys Lys
                485                 490                 495
Leu Lys Pro Gly Lys Gln Cys Ser Pro Ser Gln Gly Pro Cys Cys Thr
            500                 505                 510
Ala Gln Cys Ala Phe Lys Ser Lys Ser Glu Lys Cys Arg Asp Asp Ser
        515                 520                 525
Asp Cys Ala Arg Glu Gly Ile Cys Asn Gly Phe Thr Ala Leu Cys Pro
    530                 535                 540
Ala Ser Asp Pro Lys Pro Asn Phe Thr Asp Cys Asn Arg His Thr Gln
545                 550                 555                 560
Val Cys Ile Asn Gly Gln Cys Ala Gly Ser Ile Cys Glu Lys Tyr Gly
                565                 570                 575
Leu Glu Glu Cys Thr Cys Ala Ser Ser Asp Gly Lys Asp Asp Lys Glu
            580                 585                 590
Leu Cys His Val Cys Cys Met Lys Lys Met Asp Pro Ser Thr Cys Ala
        595                 600                 605
Ser Thr Gly Ser Val Gln Trp Ser Arg His Phe Ser Gly Arg Thr Ile
    610                 615                 620
Thr Leu Gln Pro Gly Ser Pro Cys Asn Asp Phe Arg Gly Tyr Cys Asp
625                 630                 635                 640
Val Phe Met Arg Cys Arg Leu Val Asp Ala Asp Gly Pro Leu Ala Arg
                645                 650                 655
Leu Lys Lys Ala Ile Phe Ser Pro Glu Leu Tyr Glu Asn Ile Ala Glu
```

```
            660                 665                 670
Trp Ile Val Ala His Trp Trp Ala Val Leu Leu Met Gly Ile Ala Leu
        675                 680                 685
Ile Met Leu Met Ala Gly Phe Ile Lys Ile Cys Ser Val His Thr Pro
    690                 695                 700
Ser Ser Asn Pro Lys Leu Pro Pro Pro Lys Pro Leu Pro Gly Thr Leu
705                 710                 715                 720
Lys Arg Arg Arg Pro Pro Gln Pro Ile Gln Gln Pro Gln Arg Gln Arg
                725                 730                 735
Pro Arg Glu Ser Tyr Gln Met Gly His Met Arg Arg
            740                 745
```

<210> 552
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0252

<400> 552

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 553

<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0486

<400> 553
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 554
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0351

<400> 554
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu

```
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 555
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0422

<400> 555

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1                   5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Glu Gly Gly
    130                 135                 140
Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln
145                 150                 155                 160
Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met
                165                 170                 175
```

Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser
180 185 190
Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala
195 200 205
Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly
210 215 220
Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr
225 230 235 240
Gly Val

<210> 556
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0489

<400> 556
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 557
<211> 241
<212> PRT

<213> Artificial Sequence

<220>
<223> CB0464

<400> 557
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Glu Phe Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 558
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0490

<400> 558
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu

65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 559
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0487

<400> 559
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190

```
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 560
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0268

<400> 560

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Asp Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 561
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0251

<400> 561
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 562
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0377

<400> 562
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr

```
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 563
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0244

<400> 563

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
```

Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 564
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0488

<400> 564
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 565
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0373

<400> 565
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 566
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0232

<400> 566
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met

```
                100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
            115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 567
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0082

<400> 567

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Trp
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
```

Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 568
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0274

<400> 568
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Glu Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 569
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0080

<400> 569

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Asp
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 570
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0367

<400> 570

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
```

```
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 571
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0383

<400> 571

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Leu Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
```

Val

<210> 572
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0357

<400> 572
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 573
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0387

<400> 573
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15

Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Trp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 574
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0238

<400> 574
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr

```
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 575
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0458

<400> 575

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Glu Arg Asn Arg Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 576
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0235

<400> 576
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Ala Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 577
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0381

<400> 577
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30

```
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
         35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
     50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln His Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 578
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0388

<400> 578

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
```

```
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 579
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0257

<400> 579

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Tyr Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 580
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0385

<400> 580
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Phe Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 581
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0021

<400> 581
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45

```
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Glu Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 582
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0020

<400> 582

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
```

```
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 583
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0245

<400> 583

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 584
<211> 241

<212> PRT
<213> Artificial Sequence

<220>
<223> CB0451

<400> 584
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Leu Arg Asn Ser Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 585
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0332

<400> 585
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Glu Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60

```
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 586
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0403

<400> 586

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
```

```
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Phe Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 587
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0353

<400> 587

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly Val Thr Gln Tyr Asp Gly Gly
    130                 135                 140
Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln
145                 150                 155                 160
Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met
                165                 170                 175
Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser
            180                 185                 190
Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala
        195                 200                 205
Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly
    210                 215                 220
Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr
225                 230                 235                 240
Gly Val
```

<210> 588
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0213

<400> 588
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 589
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0214

<400> 589
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80

```
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Ala Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 590
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0255

<400> 590

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
```

```
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Thr Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 591
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0423

<400> 591

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 592
<211> 241
<212> PRT
<213> Artificial Sequence

<220>

<223> CB0016

<400> 592

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Phe Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 593
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0017

<400> 593

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
```

Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Asn Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 594
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0413

<400> 594
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Phe Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val

```
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 595
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0412

<400> 595

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Leu Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 596
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0450

<400> 596
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 597
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0409

<400> 597
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ala Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110

```
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 598
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0350

<400> 598

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Glu Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
```

225 230 235 240
Val

<210> 599
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0331

<400> 599
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Asp Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 600
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0349

<400> 600
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val

```
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Asp Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 601
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0212

<400> 601

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
```

```
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asn Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 602
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0421

<400> 602

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 603
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0218

<400> 603
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Phe Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 604
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0219

<400> 604
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15

Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Ala Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 605
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0216

<400> 605
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125

```
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Val Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 606
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0252 FL

<400> 606

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
```

```
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
```

```
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 607
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0486 FL

<400> 607
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                   5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
```

Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685

```
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 608
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0351 FL

<400> 608

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
```

```
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
```

```
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 609
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0422 FL

<400> 609

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
```

```
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
```

```
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 610
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0489 FL

<400> 610

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
```

```
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
```

```
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 611
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0464 FL

<400> 611

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                   5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
```

```
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
```

```
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Glu Phe Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 612
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0490 FL

```
<400> 612
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
```

```
                100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
            115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
```

```
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 613
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0487 FL

<400> 613

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
```

```
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
```

```
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 614
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0268 FL

<400> 614

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
```

```
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
```

```
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Asp
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 615
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0251 FL

<400> 615
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
```

```
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
```

```
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 616
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0377 FL

<400> 616
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe

```
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
```

```
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 617
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0244 FL

<400> 617

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
```

```
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 618
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0488 FL

<400> 618

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
```

```
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 619

<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0373 FL

<400> 619

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
```

```
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 620
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0232 FL

<400> 620
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe

370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp

```
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 621
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0082 FL

<400> 621
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
```

```
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
            355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
        370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
            435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
        450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
            515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
        530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
            595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
        610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Trp Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
            675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
        690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
            755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
        770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
```

```
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 622
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0274 FL

<400> 622
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
```

```
                 325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Glu Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
```

785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 623
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0080 FL

<400> 623
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300

```
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Asp Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
```

```
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 624
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0367 FL

<400> 624
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
```

```
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
```

```
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 625
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0383 FL

<400> 625

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
```

```
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
```

```
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Leu Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 626
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0357 FL

<400> 626

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
```

225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn

```
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 627
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0387 FL

<400> 627

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
```

Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670

```
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Trp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 628
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0238 FL

<400> 628

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                  5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
```

```
                180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
```

```
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 629
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0458 FL

<400> 629

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
```

```
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
```

```
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Glu
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 630
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0235 FL

<400> 630

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
```

```
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
```

595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Ala Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 631
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0381 FL

<400> 631
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110

```
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
```

```
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln His Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 632
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0388 FL

<400> 632

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
```

```
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
```

```
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 633
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0257 FL

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<400> 633
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
```

```
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
```

```
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Tyr Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 634
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0385 FL

<400> 634
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
```

```
          35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
     50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
```

```
                500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
            515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
        530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Phe Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 635
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0021 FL

<400> 635
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
```

Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480

```
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Glu Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 636
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0020 FL

<400> 636

Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys

```
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 637
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0245 FL

<400> 637

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
```

```
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 638
<211> 855

<212> PRT
<213> Artificial Sequence

<220>
<223> CB0451 FL

<400> 638
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe

```
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Leu
            820                 825                 830
Arg Asn Ser Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 639
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0332 FL

<400> 639

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
```

```
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Glu
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
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Ile Lys Glu Asn Thr Gly Val
850 855

<210> 640
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0403 FL

<400> 640
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp

```
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Phe Gly Cys Ala Gln
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820 825 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 641
<211> 856
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0353 FL

<400> 641
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335

```
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly Val
            740                 745                 750
Thr Gln Tyr Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu
        755                 760                 765
Ile Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln
    770                 775                 780
Ile Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp
785                 790                 795                 800
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp
                805                 810                 815
Gly Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala
            820                 825                 830
Gln Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp
        835                 840                 845
Trp Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 642
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0213 FL

<400> 642
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
```

```
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
```

```
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 643
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0214 FL

<400> 643

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
```

```
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
```

```
Thr Gln Ala Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 644
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0255 FL

<400> 644
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
```

```
                260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
            275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
        290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
```

```
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Thr Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 645
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0423 FL

<400> 645

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
```

```
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
```

```
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 646
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0016 FL

<400> 646

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
```

```
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
```

```
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Phe Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 647
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0017 FL

<400> 647

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
```

```
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
```

```
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Asn Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Lys Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 648
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0413 FL

<400> 648

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
```

```
                    165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
                180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
            195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Phe
```

625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 649
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0412 FL

<400> 649
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140

```
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
```

```
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Leu
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 650
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0450 FL

<400> 650
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                  5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
```

```
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
```

```
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 651
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0409 FL

<400> 651

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
```

```
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
```

```
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ala
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 652
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0350 FL

<400> 652
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                  5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
```

65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys

```
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Glu
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 653
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0331 FL

<400> 653

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
```

```
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
```

```
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Asp
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 654
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0349 FL

<400> 654

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
```

```
                20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
            35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
        50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
```

```
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Asp
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 655
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0212 FL

<400> 655

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
```

```
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asn Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 656
<211> 855
<212> PRT
<213> Artificial Sequence

<220>

<223> CB0421 FL

<400> 656

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
```

```
         435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 657
<211> 855
<212> PRT

<213> Artificial Sequence

<220>
<223> CB0218 FL

<400> 657

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
```

```
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Phe Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 658
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0219 FL

<400> 658

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
```

385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Ala Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val

850 855

<210> 659
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0216 FL

<400> 659

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
```

```
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Tyr Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Val Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
```

```
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 660
<211> 313
<212> PRT
<213> Homo sapien

<220>
<223> L- Ficolin

<400> 660
Met Glu Leu Asp Arg Ala Val Gly Val Leu Gly Ala Ala Thr Leu Leu
 1               5                  10                  15
Leu Ser Phe Leu Gly Met Ala Trp Ala Leu Gln Ala Ala Asp Thr Cys
            20                  25                  30
Pro Glu Val Lys Met Val Gly Leu Glu Gly Ser Asp Lys Leu Thr Ile
        35                  40                  45
Leu Arg Gly Cys Pro Gly Leu Pro Gly Ala Pro Gly Asp Lys Gly Glu
    50                  55                  60
Ala Gly Thr Asn Gly Lys Arg Gly Glu Arg Gly Pro Pro Gly Pro Pro
65                  70                  75                  80
Gly Lys Ala Gly Pro Pro Gly Pro Asn Gly Ala Pro Gly Glu Pro Gln
                85                  90                  95
Pro Cys Leu Thr Gly Pro Arg Thr Cys Lys Asp Leu Leu Asp Arg Gly
            100                 105                 110
His Phe Leu Ser Gly Trp His Thr Ile Tyr Leu Pro Asp Cys Arg Pro
        115                 120                 125
Leu Thr Val Leu Cys Asp Met Asp Thr Asp Gly Gly Gly Trp Thr Val
    130                 135                 140
Phe Gln Arg Arg Val Asp Gly Ser Val Asp Phe Tyr Arg Asp Trp Ala
145                 150                 155                 160
Thr Tyr Lys Gln Gly Phe Gly Ser Arg Leu Gly Glu Phe Trp Leu Gly
                165                 170                 175
Asn Asp Asn Ile His Ala Leu Thr Ala Gln Gly Thr Ser Glu Leu Arg
            180                 185                 190
Val Asp Leu Val Asp Phe Glu Asp Asn Tyr Gln Phe Ala Lys Tyr Arg
        195                 200                 205
Ser Phe Lys Val Ala Asp Glu Ala Glu Lys Tyr Asn Leu Val Leu Gly
    210                 215                 220
Ala Phe Val Glu Gly Ser Ala Gly Asp Ser Leu Thr Phe His Asn Asn
225                 230                 235                 240
Gln Ser Phe Ser Thr Lys Asp Gln Asp Asn Asp Leu Asn Thr Gly Asn
                245                 250                 255
Cys Ala Val Met Phe Gln Gly Ala Trp Trp Tyr Lys Asn Cys His Val
            260                 265                 270
Ser Asn Leu Asn Gly Arg Tyr Leu Arg Gly Thr His Gly Ser Phe Ala
        275                 280                 285
Asn Gly Ile Asn Trp Lys Ser Gly Lys Gly Tyr Asn Tyr Ser Tyr Lys
    290                 295                 300
Val Ser Glu Met Lys Val Arg Pro Ala
305                 310


<210> 661
```

<211> 326
<212> PRT
<213> Homo sapien

<220>
<223> M-Ficolin

<400> 661
Met Glu Leu Ser Gly Ala Thr Met Ala Arg Gly Leu Ala Val Leu Leu
1 5 10 15
Val Leu Phe Leu His Ile Lys Asn Leu Pro Ala Gln Ala Ala Asp Thr
20 25 30
Cys Pro Glu Val Lys Val Val Gly Leu Glu Gly Ser Asp Lys Leu Thr
35 40 45
Ile Leu Arg Gly Cys Pro Gly Leu Pro Gly Ala Pro Gly Pro Lys Gly
50 55 60
Glu Ala Gly Val Ile Gly Glu Arg Gly Glu Arg Gly Leu Pro Gly Ala
65 70 75 80
Pro Gly Lys Ala Gly Pro Val Gly Pro Lys Gly Asp Arg Gly Glu Lys
85 90 95
Gly Met Arg Gly Glu Lys Gly Asp Ala Gly Gln Ser Gln Ser Cys Ala
100 105 110
Thr Gly Pro Arg Asn Cys Lys Asp Leu Leu Asp Arg Gly Tyr Phe Leu
115 120 125
Ser Gly Trp His Thr Ile Tyr Leu Pro Asp Cys Arg Pro Leu Thr Val
130 135 140
Leu Cys Asp Met Asp Thr Asp Gly Gly Gly Trp Thr Val Phe Gln Arg
145 150 155 160
Arg Met Asp Gly Ser Val Asp Phe Tyr Arg Asp Trp Ala Ala Tyr Lys
165 170 175
Gln Gly Phe Gly Ser Gln Leu Gly Glu Phe Trp Leu Gly Asn Asp Asn
180 185 190
Ile His Ala Leu Thr Ala Gln Gly Ser Ser Glu Leu Arg Val Asp Leu
195 200 205
Val Asp Phe Glu Gly Asn His Gln Phe Ala Lys Tyr Lys Ser Phe Lys
210 215 220
Val Ala Asp Glu Ala Glu Lys Tyr Lys Leu Val Leu Gly Ala Phe Val
225 230 235 240
Gly Gly Ser Ala Gly Asn Ser Leu Thr Gly His Asn Asn Asn Phe Phe
245 250 255
Ser Thr Lys Asp Gln Asp Asn Asp Val Ser Ser Ser Asn Cys Ala Glu
260 265 270
Lys Phe Gln Gly Ala Trp Trp Tyr Ala Asp Cys His Ala Ser Asn Leu
275 280 285
Asn Gly Leu Tyr Leu Met Gly Pro His Glu Ser Tyr Ala Asn Gly Ile
290 295 300
Asn Trp Ser Ala Ala Lys Gly Tyr Lys Tyr Ser Tyr Lys Val Ser Glu
305 310 315 320
Met Lys Val Arg Pro Ala
325

<210> 662
<211> 299
<212> PRT
<213> Homo sapien

<220>

<223> H-ficolin (Hakata antigen)

<400> 662

```
Met Asp Leu Leu Trp Ile Leu Pro Ser Leu Trp Leu Leu Leu Leu Gly
 1               5                  10                  15
Gly Pro Ala Cys Leu Lys Thr Gln Glu His Pro Ser Cys Pro Gly Pro
            20                  25                  30
Arg Glu Leu Glu Ala Ser Lys Val Val Leu Leu Pro Ser Cys Pro Gly
        35                  40                  45
Ala Pro Gly Ser Pro Gly Glu Lys Gly Ala Pro Gly Pro Gln Gly Pro
    50                  55                  60
Pro Gly Pro Pro Gly Lys Met Gly Pro Lys Gly Glu Pro Gly Asp Pro
65                  70                  75                  80
Val Asn Leu Leu Arg Cys Gln Glu Gly Pro Arg Asn Cys Arg Glu Leu
                85                  90                  95
Leu Ser Gln Gly Ala Thr Leu Ser Gly Trp Tyr His Leu Cys Leu Pro
            100                 105                 110
Glu Gly Arg Ala Leu Pro Val Phe Cys Asp Met Asp Thr Glu Gly Gly
        115                 120                 125
Gly Trp Leu Val Phe Gln Arg Arg Gln Asp Gly Ser Val Asp Phe Phe
    130                 135                 140
Arg Ser Trp Ser Ser Tyr Arg Ala Gly Phe Gly Asn Gln Glu Ser Glu
145                 150                 155                 160
Phe Trp Leu Gly Asn Glu Asn Leu His Gln Leu Thr Leu Gln Gly Asn
                165                 170                 175
Trp Glu Leu Arg Val Glu Leu Glu Asp Phe Asn Gly Asn Arg Thr Phe
            180                 185                 190
Ala His Tyr Ala Thr Phe Arg Leu Leu Gly Glu Val Asp His Tyr Gln
        195                 200                 205
Leu Ala Leu Gly Lys Phe Ser Glu Gly Thr Ala Gly Asp Ser Leu Ser
    210                 215                 220
Leu His Ser Gly Arg Pro Phe Thr Thr Tyr Asp Ala Asp His Asp Ser
225                 230                 235                 240
Ser Asn Ser Asn Cys Ala Val Ile Val His Gly Ala Trp Trp Tyr Ala
                245                 250                 255
Ser Cys Tyr Arg Ser Asn Leu Asn Gly Arg Tyr Ala Val Ser Glu Ala
            260                 265                 270
Ala Ala His Lys Tyr Gly Ile Asp Trp Ala Ser Gly Arg Gly Val Gly
        275                 280                 285
His Pro Tyr Arg Arg Val Arg Met Met Leu Arg
    290                 295
```

<210> 663
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0476 FL

<400> 663

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
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```
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 664
<211> 855
<212> PRT
<213> Artificial Sequence

<220>

<223> CB0477 FL

<400> 664

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
```

```
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 665
<211> 855
<212> PRT

<213> Artificial Sequence

<220>
<223> CB0478 FL

<400> 665
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415

```
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 666
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0480 FL

<400> 666
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp

385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val

850 855

<210> 667
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0481 FL

<400> 667

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
```

```
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
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Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 668
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0482 FL

<400> 668
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
```

```
                340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
            355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
        370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
```

```
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Arg Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 669
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0483 FL

<400> 669

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
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```
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
```

```
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 670
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0484 FL

<400> 670
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
```

```
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
```

```
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 671
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0485 FL

```
<400> 671
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
```

Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735

```
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Glu Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Leu Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 672
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0476 protease domain

<400> 672
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 673
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0477 protease domain

<400> 673
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 674
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0478 protease domain

<400> 674
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile

```
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 675
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0480 protease domain

<400> 675

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
```

```
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 676
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0481 protease domain

<400> 676

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 677
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0482 protease domain

<400> 677
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Arg Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 678
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0483 protease domain

<400> 678
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg

```
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 679
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0484 protease domain

```
<400> 679
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
```

```
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 680
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> CB0485 protease domain

<400> 680

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Glu Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Leu Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 681
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/K224N FL

<400> 681
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp

385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val

850 855

<210> 682
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175D/K224N FL

<400> 682

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
```

```
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
```

```
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 683
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/K224N  FL

<400> 683
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
```

```
                340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
            355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
```

```
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 684
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/G151L/K224N FL

<400> 684

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
```

```
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile
    770                 775                 780
```

```
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 685
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175R/K224N FL

<400> 685

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
```

```
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
```

```
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 686
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175K/K224N FL

<400> 686

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
```

```
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
```

```
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 687
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175H/K224N FL

<400> 687

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
```

```
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Ile
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
```

705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln His Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 688
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175K/K224F FL

<400> 688
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220

```
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
```

```
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
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<210> 689
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175R/K224F FL

<400> 689

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
```

195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp

```
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 690
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175H/K224F FL

<400> 690

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
```

Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640

Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln His Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 691
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175Y/K224F FL

<400> 691
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser

145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
565 570 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
580 585 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
595 600 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly

610 615 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625 630 635 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
645 650 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
660 665 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
675 680 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
690 695 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705 710 715 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
725 730 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
740 745 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
755 760 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile
770 775 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785 790 795 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
805 810 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
820 825 830
Arg Asn Phe Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
835 840 845
Ile Lys Glu Asn Thr Gly Val
850 855

<210> 692
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175K/K224N FL

<400> 692
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
1 5 10 15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
20 25 30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
35 40 45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
50 55 60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65 70 75 80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125

```
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
     130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
```

```
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 693
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175R/K224N  FL

<400> 693
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1               5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
```

100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545 550 555 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn

```
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855


<210> 694
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175H/K224N  FL

<400> 694
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                  5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
```

Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
85 90 95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
100 105 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
115 120 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
130 135 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145 150 155 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
165 170 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
180 185 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
195 200 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
210 215 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225 230 235 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
245 250 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
260 265 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
275 280 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
290 295 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305 310 315 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
325 330 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
340 345 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
355 360 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
370 375 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385 390 395 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
405 410 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
420 425 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
435 440 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
450 455 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465 470 475 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
485 490 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
500 505 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
515 520 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
530 535 540

```
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln His Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 695
<211> 855
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175Y/K224N FL

<400> 695

```
Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1                5                  10                  15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
```

```
     50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Pro Cys Pro Gly Gln Phe Thr Cys Arg Thr Gly Arg Cys
    450                 455                 460
Ile Arg Lys Glu Leu Arg Cys Asp Gly Trp Ala Asp Cys Thr Asp His
465                 470                 475                 480
Ser Asp Glu Leu Asn Cys Ser Cys Asp Ala Gly His Gln Phe Thr Cys
                485                 490                 495
Lys Asn Lys Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn
            500                 505                 510
Asp Cys Gly Asp Asn Ser Asp Glu Gln Gly Cys Ser Cys Pro Ala Gln
```

```
        515                 520                 525
Thr Phe Arg Cys Ser Asn Gly Lys Cys Leu Ser Lys Ser Gln Gln Cys
    530                 535                 540
Asn Gly Lys Asp Asp Cys Gly Asp Gly Ser Asp Glu Ala Ser Cys Pro
545                 550                 555                 560
Lys Val Asn Val Val Thr Cys Thr Lys His Thr Tyr Arg Cys Leu Asn
                565                 570                 575
Gly Leu Cys Leu Ser Lys Gly Asn Pro Glu Cys Asp Gly Lys Glu Asp
            580                 585                 590
Cys Ser Asp Gly Ser Asp Glu Lys Asp Cys Asp Cys Gly Leu Arg Ser
        595                 600                 605
Phe Thr Arg Gln Ala Arg Val Val Gly Gly Thr Asp Ala Asp Glu Gly
    610                 615                 620
Glu Trp Pro Trp Gln Val Ser Leu His Ala Leu Gly Gln Gly His Thr
625                 630                 635                 640
Cys Gly Ala Ser Leu Ile Ser Pro Asn Trp Leu Val Ser Ala Ala His
                645                 650                 655
Cys Tyr Ile Asp Asp Arg Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp
            660                 665                 670
Thr Ala Phe Leu Gly Leu His Asp Gln Ser Gln Arg Ser Ala Pro Gly
        675                 680                 685
Val Gln Glu Arg Arg Leu Lys Arg Ile Ile Ser His Pro Phe Phe Asn
    690                 695                 700
Asp Phe Thr Phe Asp Tyr Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro
705                 710                 715                 720
Ala Glu Tyr Ser Ser Met Val Arg Pro Ile Cys Leu Pro Asp Ala Ser
                725                 730                 735
His Val Phe Pro Ala Gly Lys Ala Ile Trp Val Thr Gly Trp Gly His
            740                 745                 750
Thr Gln Asp Gly Gly Thr Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile
        755                 760                 765
Arg Val Ile Asn Gln Thr Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile
    770                 775                 780
Thr Pro Arg Met Met Cys Val Gly Phe Leu Ser Gly Gly Val Asp Ser
785                 790                 795                 800
Cys Gln Gly Asp Ser Gly Gly Pro Leu Ser Ser Val Glu Ala Asp Gly
                805                 810                 815
Arg Ile Phe Gln Ala Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln
            820                 825                 830
Arg Asn Asn Pro Gly Val Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp
        835                 840                 845
Ile Lys Glu Asn Thr Gly Val
    850                 855
```

<210> 696
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/K224N protease domain

<400> 696

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
```

Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 697
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175D/K224N protease domain

<400> 697
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr

145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Asp Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 698
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/K224N protease domain

<400> 698
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 699
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/G151L/K224N protease domain

<400> 699
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 700
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175R/K224N protease domain

<400> 700
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45

Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 701
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175K/K224N protease domain

<400> 701
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile Thr Pro Arg Met Met Cys

```
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 702
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> Y146D/Q175H/K224N protease domain

<400> 702

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Gly Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln His Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 703
<211> 241

<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175K/K224F protease domain

<400> 703
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 704
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175R/K224F protease domain

<400> 704
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60

```
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
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<210> 705
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175H/K224F protease domain

<400> 705

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln His Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
```

```
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 706
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175Y/K224F protease domain

<400> 706

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Phe Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 707
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175K/K224N protease domain

<400> 707
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
85 90 95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
100 105 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
115 120 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
130 135 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145 150 155 160
Thr Cys Glu Asn Leu Leu Pro Gln Lys Ile Thr Pro Arg Met Met Cys
165 170 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
180 185 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
195 200 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
210 215 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225 230 235 240
Val

<210> 708
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175R/K224N protease domain

<400> 708
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
1 5 10 15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
20 25 30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
35 40 45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
50 55 60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65 70 75 80

```
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Arg Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 709
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175H/K224N protease domain

<400> 709

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln His Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
```

```
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

<210> 710
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> I41T/Y146D/G151L/Q175Y/K224N protease domain

<400> 710

```
Val Val Gly Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val
 1               5                  10                  15
Ser Leu His Ala Leu Gly Gln Gly His Thr Cys Gly Ala Ser Leu Ile
            20                  25                  30
Ser Pro Asn Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg
        35                  40                  45
Gly Phe Arg Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu
    50                  55                  60
His Asp Gln Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu
65                  70                  75                  80
Lys Arg Ile Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr
                85                  90                  95
Asp Ile Ala Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met
            100                 105                 110
Val Arg Pro Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly
        115                 120                 125
Lys Ala Ile Trp Val Thr Gly Trp Gly His Thr Gln Asp Gly Gly Thr
    130                 135                 140
Leu Ala Leu Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr
145                 150                 155                 160
Thr Cys Glu Asn Leu Leu Pro Gln Tyr Ile Thr Pro Arg Met Met Cys
                165                 170                 175
Val Gly Phe Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly
            180                 185                 190
Gly Pro Leu Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly
        195                 200                 205
Val Val Ser Trp Gly Asp Gly Cys Ala Gln Arg Asn Asn Pro Gly Val
    210                 215                 220
Tyr Thr Arg Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly
225                 230                 235                 240
Val
```

□