CELL SURFACE RECEPTOR ISOFORMS AND METHODS OF IDENTIFYING AND USING THE SAME

RELATED APPLICATIONS

Benefit of priority is claimed to U.S. Provisional Application Serial No. 60/666,825 to Pei Jin and H. Michael Shepard, filed March 30, 2005, entitled "CELL SURFACE RECEPTOR ISOFORMS AND METHODS OF IDENTIFYING AND USING SAME;" to U.S. Provisional Application Serial No. 60/571,289 to Pei Jin, filed May 14, 2004, entitled "CELL SURFACE RECEPTOR ISOFORMS AND METHODS OF IDENTIFYING AND USING SAME,"; and to U.S. Provisional Application Serial No. 60/580,990 to Pei Jin, filed June 18, 2004, entitled "CELL SURFACE RECEPTOR ISOFORMS AND METHODS OF IDENTIFYING AND USING SAME."

This application also is related to U.S. application Serial No. 10/846,113, filed May 14, 2004, and to corresponding published International PCT application No. WO 05/016966, published February 24, 2005, entitled "INTRON FUSION PROTEINS, AND METHODS OF IDENTIFYING AND USING SAME." This application also is related to U.S. Application Serial No. 11/129,746 to Pei Jin and H. Michael Shepard, entitled "CELL SURFACE RECEPTOR ISOFORMS AND METHODS OF IDENTIFYING AND USING THE SAME," filed the same day herewith.

Where permitted, the subject matter of each of these applications, provisional applications and international applications is incorporated herein by reference thereto.

FIELD OF THE INVENTION

Isoforms of cell surface receptors, including isoforms of receptor tyrosine kinases and pharmaceutical compositions containing receptor tyrosine kinase isoforms are provided. The cell surface receptor isoforms and compositions containing them can be used in methods of treatment of diseases, such as cancer and inflammatory disease.

BACKGROUND

Cell signaling pathways involve a network of molecules including polypeptides and small molecules that interact to relay extracellular, intercellular and intracellular signals. Such pathways interact like a relay, handing off signals from

one member of the pathway to the next. Modulation of one member of the pathway can be relayed through the signal transduction pathway, resulting in modulation of activities of other pathway members and modulating outcomes of such signal transduction such as affecting phenotypes and responses of a cell or organism to a signal. Diseases and disorders can involve misregulated or changes in modulation of signal transduction pathways. A goal of drug development is to target such misregulated pathways to restore more normal regulation in the signal transduction pathway.

Receptor tyrosine kinases (RTKs) are among the polypeptides involved in many signal transduction pathways. RTKs play a role in a variety of cellular processes, including cell division, proliferation, differentiation, migration and metabolism. RTKs can be activated by ligands. Such activation in turn activates events in a signal transduction pathway, such as by triggering autocrine or paracrine cellular signaling pathways, for example, activation of second messengers, which results in specific biological effects. Ligands for RTKs specifically bind to the cognate receptors.

RTKs have been implicated in a number of diseases including cancers such as breast and colorectal cancers, gastric carcinoma, gliomas and mesodermal-derived tumors. Disregulation of RTKs has been noted in several cancers. For example, breast cancer can be associated with amplified expression of p185-HER2. RTKs also have been associated with diseases of the eye, including diabetic retinopathies and macular degeneration. RTKs also are associated with regulating pathways involved in angiogenesis, including physiologic and tumor blood vessel formation. RTKs also are implicated in the regulation of cell proliferation, migration and survival.

The human epidermal growth factor receptor 2 gene (HER-2; also referred to as ErbB2) encodes a receptor tyrosine kinase that has been implicated as an oncogene. HER-2 has a major mRNA transcript of 4.5 Kb that encodes a polypeptide of about 185 kD (P185HER2). P185HER2 contains an extracellular domain, a transmembrane domain and an intracellular domain with tyrosine kinase activity. Several polypeptide forms are produced from the HER-2 gene and include polypeptides generated by proteolytic processing and forms generated from

alternatively spliced RNAs. Herstatins and fragments thereof are HER-2 binding proteins, encoded by the HER-2 gene. Herstatins (also referred to as p68HER-2) are encoded by an alternatively spliced variant of the gene encoding the p185-HER2 receptor. For example, one Herstatin occurs in fetal kidney and liver, and includes a 79 amino acid intron-encoded insert, relative to the membrane-localized receptor, at the C terminus (see U.S. Patent No. 6,414,130 and U.S. Published Application No. 20040022785). Several Herstatin variants have been identified (see, *e.g.*, U.S. Patent No. 6,414,130; U.S. Published Application No. 20040022785, U.S. appln. Serial No. 09/234,208; U.S. appln. Serial No.09/506,079; published international application Nos. WO0044403 and WO0161356). Herstatins lack an epidermal growth factor (EGF) homology domain and contain part of the extracellular domain, typically the first 340 amino acids, of p185-HER2. Herstatins contain subdomains I and II of the human epidermal growth factor receptor, the HER-2 extracellular domain and a C-terminal domain encoded by an intron. The resulting herstatin polypeptides typically contain 419 amino acids (340 amino acids from subdomains I and II, plus 79 amino acids from intron 8). The herstatin proteins lack extracellular domain IV, as well as the transmembrane domain and kinase domain.

In contrast, positive acting EGFR ligands, such as the epidermal growth factor and transforming growth factor-alpha, possess such domains. Additionally, binding of a herstatin does not activate the receptor. Herstatins can inhibit members of the EGF-family of receptor tyrosine kinases as well as the insulin-like growth factor-1 (IGF-1) receptor and other receptors. Herstatins prevent the formation of productive receptor dimers (homodimers and heterodimers) required for transphosphorylation and receptor activation. Alternatively or additionally, herstatin can compete with a ligand for binding to the receptor terminus (see, U.S. Patent No. 6,414,130; U.S. Published Application No. 20040022785, U.S. appln. Serial No. 09/234,208; U.S. appln. Serial No.09/506,079; published international application Nos. WO0044403 and WO0161356).

The tumor necrosis factor family of receptors (TNFRs) is another example of a family of receptors involved in signal transduction and regulation. The TNF ligand and receptor family regulate a variety of signal transduction pathways including those

involved in cell differentiation, activation, and viability. TNFRs contain an extracellular domain, including a ligand binding domain, a transmembrane domain and an intracellular domain that participates in signal transduction. Additionally, TNFRs are typically trimeric proteins that trimerize at the cell surface. TNFRs play a role in inflammatory diseases, central nervous system diseases, autoimmune diseases, airway hyper-responsiveness conditions such as in asthma, rheumatoid arthritis and inflammatory bowel disease. TNFRs also play a role in infectious diseases, such as viral infection.

The TNF family of receptors (TNFR) exhibit homology among the extracellular domains. Some of these receptors initiate apoptosis, some initiate cell proliferation and some initiate both activities. Signaling by this family requires clustering of the receptors by trimeric ligand and subsequent association of proteins with the cytoplasmic region of the receptors. The TNFR family contains a sub family with homologous cytoplasmic 80-amino-acid domains. This domain is referred to as a death domain (DD), so named because proteins that contain this domain are involved in apoptosis. The distinction between members of the TNFR family is exemplified by two TNFRs coded by distinct genes. TNFRI (55 kDa) signals the initiation of apoptosis and the activation of the transcription factor NFkB. TNFRII (75 kDa) functions to signal activation of NFkB but not the initiation of apoptosis. TNFRI contains a DD; TNFRII does not.

Because of their involvement in a variety of diseases and conditions, cell surface receptors (CSRs) such as RTKs and TNFRs are targets for therapeutic intervention. Small molecule therapeutics that target RTKs have been designed. While it may be possible to design small molecules as therapeutics that target cell surface receptors and/or other receptors, there, however, are a number of limitations with such strategies. Small molecules can be limited to interactions with one receptor and thus unable to address conditions where multiple family members may be misregulated. Small molecules also can be promiscuous and affect receptors other than the intended target. Additionally, some small molecules bind irreversibly or substantially irreversibly to the receptors (*i.e.* subnanomolar binding affinity). The merits of such approaches have not been validated. Antibodies against receptor

and/or receptor ligands can be used as therapeutics. Antibody treatments, however, can result in an immune response in a subject and thus, such treatments often need extensive tailoring to avoid complications in treatment. Thus, there exists an unmet need for therapeutics for treatment of diseases, including cancers and other diseases involving undesirable cell proliferation and inflammatory reactions, involving cell surface receptors that exhibit RTK activity and/or other cell surface proteins. Accordingly, among the objects herein, it is an object to provide such therapeutics and methods for identifying or discovering candidate therapeutics and methods of treatment.

SUMMARY

Therapeutic molecules for treating diseases and disorders involving the signal transduction pathways and other cell surface receptor interactions are provided. The therapeutic molecules particularly target RTKs that participated in signal transduction pathways, including those involved in angiogenesis and neovascularization and cell proliferation, particular aberrant angiogenesis, neovascularization and/or cell proliferation. Also provided are compositions containing the molecules and methods for treating diseases and conditions, particularly diseases that include or exhibit or are manifested by aberrant angiogenesis, neovascularization and/or cell proliferation. Also provided are methods for identifying candidate therapeutics and methods of treatment by administering therapeutic molecules and compositions. The therapeutic molecules can be used for treating any such disease or disorder and exhibit activity, whereby such treatment is effective. Diseases and disorders including proliferative disorders, include tumors, immune disorders and inflammatory disorders. Targets include cells involved in angiogenesis and neovascularization and cells involved in inflammatory responses, cancers and other such disorders. Activity includes modulation of the activity of a cell surface receptor, including RTKs and TNFRs, such as by directly altering the activity by virtue of interaction with the receptor or indirectly by interacting with ligands.

Among the therapeutic molecules provided herein are those that modulate the activity of cellular receptors of angiogenic factors (positive and negative), which serve as points of intervention in a plurality of disease processes. Examples of

situations in which 'too much' angiogenesis is bad include angiogenesis that supplies blood to tumor foci, or to other sites of disease (such as to the human eye in diabetes). In these cases, therapeutic molecules provided herein that inhibit the process are employed.

Activities of the receptor tyrosine kinase (RTK) or TNFR (or other cell surface receptors) modulated by the therapeutic molecules provided herein include, but are not limited to, for example, one or more of dimerization, homodimerization, hetero-dimerization, trimerization, kinase activity, autophosphorylation of the receptor tyrosine kinase, transphosphorylation of the receptor tyrosine kinase, phosphorylation of a signal transduction molecule, ligand binding, competition with the receptor tyrosine kinase for ligand binding, signal transduction, interaction with a signal transduction molecule, induction of apoptosis, receptor-associated kinase activity, receptor-associated protease activity, membrane association and membrane localization. Modulation includes, for example, inhibition (such as activity as an antagonist) of an activity and also enhancement (such as activity as an agonist) of an activity. By virtue of modulation of such activity the effects of such receptors are modulated or otherwise modified.

The therapeutic molecules provided herein typically are polypeptides or peptidomimetics (including polypeptides with modified bonds) or other modified forms of polypeptides designed, for example, for improved bioavailability, delivery, stability, resistance to proteases and other properties. Contemplated are modifications of the molecules with changes that alter properties, such as bioavailability, protein stability and other such properties, for their use as therapeutics.

Exemplary of the molecules are polypeptides. Also included are allelic variants of any of the polypeptides. The allelic variants include any of the variants of the receptor, particularly variants in an extracellular domain, present in a population of the mammal in which a particular receptor occurs. Chimeric molecules, conjugates and conjugates of intron portions of the intron fusion proteins also are provided. The chimeric molecules and conjugates can include portions from molecules with different ligand binding and/or receptor interacting specificities. For example, conjugates or chimeras that contain an extracellular domain or portion thereof linked directly or

indirectly to an intron region, such as an intron of a herstatin, are provided. The chimeras and conjugates include portions from CSR isoforms provided herein and known to those of skill in the art including any described in U.S. Provisional Application Serial No. 60/571,289, U.S. Provisional Application Serial No. 60/580,990, U.S. application Serial No. 10/846,113, published International PCT application No. WO 05/016966, U.S. Patent No. 6,414,130; U.S. Published Application No. 20040022785, U.S. appln. Serial No. 09/234,208; U.S. appln. Serial No.09/506,079; published international application Nos. WO0044403 and WO0161356.

Isolated polypeptides and variants thereof are provided. The polypeptides are isoforms of cell surface receptors (CSR isoforms) and chimeras and conjugates thereof. Some CSR isoforms, such as intron fusion proteins, are missing all or part of a functional domain or other structural feature such that the activity of the domain is reduced or eliminated and/or a structure is altered compared to the full-length cognate receptor. Other examples include intron fusion proteins in which the rearrangements that occur during alternative splicing can result in either positive or negatively acting molecules. In particular, among the polypeptides provided herein are soluble or non-membrane bound forms of receptors. The polypeptides include a sequence of amino acids that has at least 80%, 85%, 90% or 95% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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, and 226 and allelic variations thereof. Such homology is exhibited along at least 70%, 80%, 85%, 90%, 95%, 97% or 100% of the full-length of the polypeptide. Sequence identity is compared along the full length of the polypeptide represented by each SEQ ID to the full length sequence of the isolated polypeptide, and each of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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, and 226 is a cell surface receptor isoform. Exemplary of such polypeptides are isolated

polypeptides containing the sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 and 155 are provided as are isolated polypeptides that have the sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 155, 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, and 226. Also provided are chimeras of these molecules and also chimeras of these molecules and herstatins.

Provided are isolated polypeptides that are receptor isoforms and that contain at least one domain of a cell surface receptor linked to at least one amino acid encoded by an intron of a gene encoding a cognate cell surface receptor. The cell surface receptor is selected from among DDR1 (discoidin domain receptor) , KIT (receptor for c-kit), FGFR-1, FGFR-2, FGFR-4, (fibroblast growth factor receptors 1, 2 and 4) TNFR2 (tumor necrosis factor receptor), VEGFR-1, VEGFR-2, VEGFR-3, (vascular endothelial growth factor receptors 1,2, and 3), RON (recepteur d'origine nantais; also known as macrophage stimulating 1 receptor), MET (also known as hepatocyte growth factor receptor), TEK (endothelial-specific receptor tyrosine kinase), Tie-1 (tyrosine kinase with immunoglobulin and epidermal growth factor homology domains receptor), CSF1R (colony stimulating factor 1 receptor), PDGFR-B (platelet-derived growth factor receptor B), EphA1, EphA2, and EphB1 (erythropoietin-producing hepatocellular receptor A1, A2 and B1, respectively). Exemplary of such polypeptides are those that contain the sequence of amino acids selected from among the sequences of amino acids set forth in SEQ ID NOS: 91, 93, 95,115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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, and 226.

Also provided are isolated polypeptide that are cell surface receptors that lack at least part of a transmembrane domain such that the resulting polypeptide is not membrane localized or bound and it modulates an activity, including a biological

activity, of the cell surface receptor. The polypeptides can include exon insertions. Among these are cell surface receptor isoforms selected from among isoforms of FGFR-4, KIT and TNFR. Exemplary of the isolated polypeptides are those that have at least 80%, 85%, 90% , 95%, 97%, or 100% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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, and 226. Sequence identity is compared along the full length of each SEQ ID to the sequence of the full length of the isolated polypeptide. The isolated polypeptides can further lack a cell surface receptor cytoplasmic domain.

Also provided are isolated polypeptides that contain an intron-encoded sequence of amino acids and lack a cell surface receptor cytoplasmic domain. The intron is an intron and is selected from among nucleic acids KIT, FGFR-4, TNFR2, VEGFR-1, RON, TEK, Tie-1, and EphA1, or is an intron from any of SEQ ID NOS: 91, 93, 95, 121, 123, 129, 131, 133, 135, 137, 139, 141, 149, 151, or 153. Also provided are polypeptides that further lack a transmembrane domain. Among these are isolated polypeptides that modulate an activity or function of a cell surface receptor. These polypeptides include TNFR isoforms, such as, but not limited to, TNFR1, TNFR2 and TNFRrp, the low-affinity nerve growth factor receptor, Fas antigen, CD40, CD27, CD30, 4-1BB, OX40, DR3, DR4, DR5, and herpes virus entry mediator (HVEM).

Also provided are chimeric intron fusion protein isoforms that contain an N-terminal portion that effects binding to a CSR linked to an intron, such as the intron or a portion thereof whereby the resulting chimera modulates, particularly, inhibits, an activity of one or more CSRs. The chimeras include N-terminal and/or intron portions of any of the isoforms provided herein and also a herstatin, linked to an intron from a different intron fusion protein isoform. The portions of the chimeras can be linked via a linker or via 2 or more amino acids. Alternatively, the chimera can be a chemical conjugate.

Also provided are CSR isoforms conjugates and chimeras in which the N-terminal portion and intron-encoded portion are linked directly or via a linker and are from the same or a different CSR isoforms, including any provided herein, a herstatin or any other CSR. The two portions can be linked via a linker, such as a polypeptide or chemical linker. The isoform conjugates modulate, typically inhibit, the activity of one or more CSRs. The CSRs include those that participate in signal transduction, particularly CSRs involved in pathways that participate in angiogenesis, inflammatory responses and cell proliferation (see, *e.g.*, Figure 1).

Provided herein are CSR isoforms that contain at least one domain of a CSR receptor and lack one or more amino acids of another domain of the CSR receptor such as the transmembrane domain and/or protein kinase domain, whereby an activity is reduced or abolished compared to the CSR. CSR isoforms include polypeptides that contain an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the CSR. For example, a CSR isoform can contain at least one domain of the CSR receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding the CSR. Among the CSR isoforms provided herein are polypeptides that contain one or more domains of an Ephrin (Eph) receptor, a fibroblast growth factor (FGF) receptor, a DDR receptor, a MET receptor, a RON receptor, a TEK/TIE receptor, a VEGF receptor, PDGF receptor, CSF1 receptor, a KIT receptor and a TNFR receptor.

Provided herein are EphA isoforms. The isoforms are isolated polypeptides that contain at least one domain of an EphA receptor. The polypeptides contain an ephrin ligand binding domain and lack one or more amino acids corresponding to the transmembrane domain of the EphA receptor, whereby the membrane localization of the polypeptide is reduced or abolished compared to the EphA receptor. Included are polypeptides where the EphA receptor is selected from among EphA1, EphA2, EphA3, EphA4, EphA5, EphA6, EphA7, and EphA8. In one example, such polypeptides include a sequence as set forth in any one of SEQ ID NO: 253 – 260 or an allelic variant thereof. The allelic variant can be an allelic variation present in any one of SEQ ID NOS: 289-293. EphA isoforms include polypeptides that lack all or

part of a protein kinase domain compared to the EphA receptor and/or that lack all or part of a Sterile Alpha Motif domain (SAM) compared to the EphA receptor.

In one example, an EphA isoform has at least one domain of an EphA1 receptor as set forth in SEQ ID NO:253. Such isoforms include EphA1 isoforms where the polypeptide lacks one or more amino acids of a protein kinase domain of the EphA1 receptor, whereby the kinase activity of the polypeptide is reduced or abolished compared to the EphA1 receptor. EphA1 isoforms also include polypeptides that have at least 80% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 149, 151 and 153 or that contain the amino acid sequence set forth in any of SEQ ID NOS: 149, 151 and 153 or an allelic variant thereof. Allelic variants include the allelic variations as set forth in SEQ ID NO: 289. EphA1 isoforms include polypeptides that contain the same number of amino acids as set forth in any of SEQ ID NOS: 149, 151 and 153.

Provided herein are EphA2 isoforms. EphA2 isoforms include at least one domain of an EphA2 receptor as set forth in SEQ ID NO:254, where the polypeptide lacks one or more amino acids of a transmembrane domain and protein kinase domain compared to the EphA2 receptor, whereby the membrane localization and the protein kinase activity of the polypeptide are reduced or abolished compared to the EphA2 receptor. EphA2 isoforms include polypeptides that contain one or more amino acids of a fibronectin domain compared to the EphA2 receptor. Examples of EphA2 isoforms also include polypeptides that have at least 80% sequence identity with a sequence of amino acids as set forth in SEQ ID NO: 168 or contains the amino acid sequence set forth in SEQ ID NO: 168 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations as set forth in SEQ ID NO: 290. EphA2 isoforms include isoforms that contain the same number of amino acids as set forth in the SEQ ID NO:168.

Also provided herein are EphB isoforms that include polypeptides lacking one or more amino acids of a transmembrane domain compared to the EphB receptor, whereby the membrane localization of the polypeptide is reduced or abolished compared to the EphB receptor. Among the EphB isoforms provided are those where the EphB receptor is selected from EphB1, EphB2, EphB3, EphB4, EphB5, and

EphB6 and where the EphB receptor comprises a sequence as set forth in any one of SEQ ID NOS: 261-265 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NOS: 294-298. Exemplary EphB isoforms include isoforms that lack one or more amino acids of a protein kinase domain of the EphB receptor, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the EphB receptor and isoforms that lacks one or more amino acids of a Sterile Alpha Motif domain (SAM) of the EphB receptor. In one example, an EphB1 isoform includes an ephrin binding domain. EphB isoforms also include isoforms that lack one or more amino acids of a fibronectin domain of the EphB receptor. Among the EphB isoforms provided herein are isoforms that have at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 155, 170, 172 and 174 and isoforms that contain the amino acid sequence as set forth in any of SEQ ID NOS: 155, 170, 172 and 174 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NOS: 294 and 297. EphB isoforms include isoforms that contain the same number of amino acids as set forth in any of SEQ ID NOS: 155, 170, 172 and 174.

FGFR isoforms are provided herein. Included are FGFR isoforms that contain at least one domain of an FGFR-1, wherein the polypeptide comprises an immunoglobulin domain corresponding to amino acids 253 – 357 of FGFR-1 set forth in SEQ ID NO:268 and lacks all of a transmembrane domain corresponding to amino acids 375 – 397 of the FGFR-1. FGFR isoforms also include isoforms that lack one or more amino acids of a protein kinase domain of FGFR-1, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the FGFR-1 and/or that contain one or more amino acids of an immunoglobulin domain corresponding to amino acids 156 – 246 of FGFR-1. FGFR isoforms provided include isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 119 or 176 and isoforms that contain any of SEQ ID NOS: 119 and 176 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NO: 300. FGFR-1 isoforms include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 119 and 176.

Also provided are FGFR-2 isoforms that have at least one domain of an FGFR-2 as set forth in SEQ ID NO: 269, where the polypeptide lacks a transmembrane domain and a protein kinase domain compared to FGFR-2, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to FGFR-2. Such isoforms include polypeptides that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 178, 180, 182 and 184 and isoforms that contain the amino acid sequence set forth in SEQ ID NOS: 178, 180, 182 or 184 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NO: 301. FGFR-2 isoforms include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 178, 180, 182 or 184. Exemplary FGFR-2 isoforms also include isoforms that lack an immunoglobulin domain corresponding to amino acids 41-125 of the FGFR-2.

FGFR-4 isoforms are provided herein that contain at least one domain of an FGFR-4, such as an immunoglobulin domain corresponding to amino acids 249 – 351of the FGFR-4 set forth in SEQ ID NO:271 and lack a transmembrane domain and protein kinase domain of the FGFR-4, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to FGFR-4. FGFR isoforms include isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 121 and isoforms that contain the amino acid sequence set forth in SEQ ID NO: 121 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NO: 303. FGFR-4 isoforms include isoforms that have the same number of amino acids as set forth in SEQ ID NO: 121.

Provided herein are DDR1 isoforms, that are polypeptides that contain at least one domain of a DDR1 as set forth in SEQ ID NO: 250, where the polypeptide lacks a transmembrane domain and a protein kinase domain compared to the DDR1, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to DDR1, and the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 115 or 117. DDR1 isoforms include isoforms that contain the amino acid sequence set forth in SEQ ID

NOS: 115 or 117 or an allelic variant thereof, such as but not limited to the allelic variations as set forth in SEQ ID NO: 286. DDR1 isoforms include isoforms that have the same number of amino acids as set forth in SEQ ID NOS: 115 or 117.

Also provided herein are MET receptor isoforms that are polypeptides which contain at least one domain of a MET receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding MET, where the polypeptide lacks a transmembrane domain, protein kinase domain and at least one additional domain compared to a MET receptor set forth in SEQ ID NO:274, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to the MET receptor. MET receptor isoforms include isoforms where the additional domain lacking as compared to the MET receptor is a Sema domain, a plexin domain or an IPTG/TIG domain. MET receptor isoforms include isoforms that have at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214 and isoforms that contain the amino acid sequence set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NO: 306. MET isoforms include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214.

RON receptor isoforms are provided herein. RON receptor isoforms include polypeptides that have a plexin domain of the RON receptor as set forth in SEQ ID NO: 277; and lack a transmembrane domain of the RON receptor, whereby the membrane localization of the polypeptide is reduced or abolished compared to the RON receptor. RON receptor isoforms include isoforms that lack one or more amino acids of a protein kinase domain compared to the RON receptor as set forth in SEQ ID NO: 277, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the RON receptor and/or contain one or more amino acids of at least one IPTG/TIG domain of the RON receptor. RON receptor isoforms include isoforms that have at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 216, 218 and 220 and isoforms that contain the

amino acid sequence set forth in any of SEQ ID NOS: 216, 218 and 220 or an allelic variant thereof, such as but not limited to allelic variations set forth in SEQ ID NO: 308. RON receptor isoforms also include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 216, 218 and 220.

Provided herein are TEK isoforms that contain at least one domain of a TEK receptor as set forth in SEQ ID NO: 278, where the isoform lacks a transmembrane domain, and a protein kinase domain, whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the TEK receptor; and lacks one or more amino acids of at least one fibronectin domain compared to the TEK receptor. TEK isoforms include isoforms where the fibronectin domain lacking corresponds to amino acids 444 – 529, 543 – 626, or 639 – 724 of SEQ ID NO: 278 and where one or more amino acids of the three fibronectin domains of the TEK receptor corresponding to amino acids 444 – 529, 543 – 626, and 639 – 724 of SEQ ID NO: 278 is lacking. TEK isoforms include isoforms that have at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 131 and 133 and isoforms that contain the amino acid sequence set forth in any of SEQ ID NOS: 131 and 133 or an allelic variant thereof, such as but not limited to allelic variations as set forth in SEQ ID NO: 309. Tek isoforms also include isoforms that contain the same number of amino acids as set forth in any of SEQ ID NOS: 131 and 133.

Tie receptor isoforms are provided herein that contain all or part of at least one domain of a Tie-1 receptor as set forth in SEQ ID NO: 279, where the isoform lacks a transmembrane domain and a protein kinase domain compared to the Tie-1 receptor, whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the Tie-1 receptor; and the isoform contains an amino acid sequence as set forth in any of SEQ ID NOS: 135, 137, 139, 141, 143 and 222 or an allelic variant thereof. Allelic variants include, but are not limited to, allelic variations set forth in SEQ ID NO: 310. Tie receptor isoforms include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 135, 137, 139, 141, 143 and 222.

Provided herein are VEGFR isoforms. VEGFR isoforms include VEGFR-1 isoforms that contain a sequence of amino acids that has at least 80% sequence identity with the sequence of amino acids as set forth in SEQ ID NO:123 and that lack a transmembrane domain and a protein kinase domain compared to the VEGFR-1 receptor set forth in SEQ ID NO: 282. Such isoforms include polypeptides that contain the amino acid sequence set forth in SEQ ID NO: 123 or an allelic variant thereof and isoforms that contain the same number of amino acids as set forth in any of SEQ ID NO: 123. VEGFR isoforms include VEGFR-2 and VEGFR-3 isoforms that contain at least one domain of a VEGFR set forth in any of SEQ ID NOS:283 and 284, where the polypeptide lacks one or more amino acids of a transmembrane domain of the VEGFR, whereby the membrane localization of the polypeptide is reduced or abolished compared to the VEGFR. VEGFR-2 and VEGFR-3 isoforms also include isoforms that lack one or more amino acids of a protein kinase domain, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the VEGFR and isoforms that lack one or more amino acids of an immunoglobulin domain compared to the VEGFR. VEGFR-2 and VEGFR-3 isoforms include polypeptides that have at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 125, 127, 224 and 226 and polypeptides that contain the amino acid sequence set forth in any of SEQ ID NOS: 125, 127, 224 and 226 or an allelic variant thereof. Allelic variants can include, but are not limited to the allelic variations as set forth in SEQ ID NO: 313 and 314. VEGFR-2 and VEGFR-3 isoforms also include isoforms that have the same number of amino acids as set forth in any of SEQ ID NOS: 125, 127, 224 and 226.

PDGFR isoforms are provided herein. Included are PDGFR isoforms that contain at least one domain of a PDGFR-B as set forth in SEQ ID NO: 276, wherein the polypeptide lacks one or more amino acids of a transmembrane domain of the PDGFR-B, whereby the membrane localization of the polypeptide is reduced or abolished compared to the PDGFR-B. PDGFR isoforms also include isoforms that lack one or more amino acids of a protein kinase domain of the PDGFR-B, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the PDGFR-B and isoforms that contain one or more amino acids of an immunoglobulin

domain of the PDGFR-B. Also included are PDGFR isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 147 and isoforms that contain the amino acid sequence set forth in SEQ ID NO: 147 or an allelic variant thereof. Allelic variants can include, but are not limited to the allelic variations as set forth in SEQ ID NO: 307. PDGFR isoforms also include isoforms that have the same number of amino acids as set forth in SEQ ID NO: 147.

Also provided herein are CSF1R isoforms that contain at least one domain of a CSF1R as set forth in SEQ ID NO: 249, where the polypeptide lacks one or more amino acids of a transmembrane domain of the CSF1R, whereby the membrane localization of the polypeptide is reduced or abolished compared to the CSF1R. CSF1R isoforms also include isoforms that lack one or more amino acids of a protein kinase domain of the CSF1R, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the CSF1R and isoforms that contain one or more amino acids of an immunoglobulin domain of the CSF1R. Included are CSF1R isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 145 and isoforms that contain the amino acid sequence set forth in SEQ ID NOS: 145 or an allelic variant thereof, such as but not limited to allelic variations as set forth in SEQ ID NO: 285. Exemplary CSF1R isoforms also include isoforms that contain the same number of amino acids as set forth in SEQ ID NO: 145.

KIT receptor isoforms are provided herein. Included are KIT receptor isoforms that contain at least one domain of a KIT receptor as set forth in SEQ ID NO:273 and lack one or more amino acids of a transmembrane domain and a protein kinase domain of the KIT receptor, whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the KIT receptor and isoforms that contain at least one immunoglobulin domain of the KIT receptor. KIT isoforms include isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 93 and isoforms that contain the amino acid sequence set forth in SEQ ID NO: 93 or an allelic variant thereof, such as but not limited to the allelic variations as set forth in SEQ ID NO:

305. KIT receptor isoforms include isoforms that have the same number of amino acids as set forth in SEQ ID NO: 93.

Provided herein are TNFR isoforms that contain at least one cysteine rich c6 domain of a TNFR as set forth in SEQ ID NOS:280 or 281 and lack all of the transmembrane domain of the TNFR, whereby the membrane localization of the polypeptide is reduced or abolished compared to the TNFR. TNFR isoforms include isoforms that contain at least two cysteine rich c6 domains of the TNFR. TNFR isoforms also include isoforms that have at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 95 and isoforms that contain the sequence set forth in SEQ ID NO: 95 or an allelic variant thereof. Allelic variation includes but is not limited to allelic variations as set forth in SEQ ID NO: 312. TNFR isoforms also include isoforms that have the same number of amino acids as set forth in SEQ ID NO: 95.

The isolated polypeptides (*e.g*, CSR isoforms) can be encoded by a gene in a mammal, particularly a human, and can be isolated from a mammalian cell or prepared from nucleic acid cloned from such cell or can be synthesized from nucleic acid prepared by any means or can be synthesized as polypeptides. Exemplary mammals include humans and other primates, horses, cattle, dogs, cats and other domesticated animals, and rodents, such as rats and mice. The isolated polypeptides can be identified by the methods provided herein, known to those of skill in the art and/ or also in, for example, copending application U.S. application Serial No. 10/846,113 and published PCT application No. WO 2005/016966.

Also provided are pharmaceutical compositions that contain any of the isolated polypeptides or combinations thereof. Included among the compositions are those that contain a polypeptide that complexes with a receptor tyrosine kinase or a tumor necrosis factor receptor. The pharmaceutical compositions can be used to treat diseases that include inflammatory diseases, immune diseases, cancers, and other diseases that manifest aberrant angiogenesis or neovascularization or cell proliferation. Cancers include breast, lung, colon, gastric cancers, pancreatic cancers and others. Inflammatory diseases, include, for example, diabetic retinopathies and/or neuropathies and other inflammatory vascular complications of diabetes,

autoimmune diseases, including autoimmune diabetes, atherosclerosis, Crohn's disease, diabetic kidney disease, cystic fibrosis, endometriosis, diabetes-induced vascular injury, inflammatory bowel disease, Alzheimer's disease and other neurodegenerative diseases, and other diseases known to those of skill in the art that involve proliferative responses, immune responses and inflammatory responses and others in which RTKs, particularly those noted in Figure 1 and throughout the disclosure herein are implicated, involved or in which they participate.

Also provided are nucleic acid molecules encoding any of the polypeptides. Vectors containing the nucleic acid molecules are provided as are cells containing the vectors or nucleic acid molecules. Among the nucleic acid molecules provided are those that contain an intron and an exon, where the intron contains a stop codon; the nucleic acid molecule encodes an open reading frame that spans an exon intron junction; and the open reading frame terminates at the stop codon in the intron. The intron can encode one or more amino acids of the encoded polypeptide or the codon can be a first codon (and possibly the only codon) in the intron.

Also provided are nucleic acid molecules that contain a sequence of nucleotides that has at least 90% sequence identity with a sequence of nucleotides set forth in any of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, and 225 or an allelic variant thereof. Sequence identity is compared along the full length of each SEQ ID to the full length sequence of the isolated nucleic acid molecule, and each of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, and 225 is a cell surface receptor isoform. In particular, nucleic acid molecules containing the sequence of nucleotides set forth in any of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, and 225 are

provided. Also provided are vectors containing any of the nucleic acid molecules and cells containing the nucleic acid molecules or vectors.

Pharmaceutical compositions containing the nucleic acid molecules and/or vectors are provided. Such compositions can be used in methods of gene therapy, including *in vivo* methods and *ex vivo* methods.

Methods of treating a disease or condition by administering any of the pharmaceutical compositions are provided. Diseases or conditions include, but are not limited to, for example, cancers, inflammatory diseases, infectious diseases, angiogenic-related conditions, other cell proliferative conditions, immune disorders and neurodegenerative diseases. Also included are methods of treatment where the pharmaceutical compositions contain one or more polypeptides that inhibit(s) angiogenesis, cell proliferation, cell migration, viral entry, viral infection, tumor cell growth or tumor cell metastasis.

Exemplary of diseases and disorders are any of rheumatoid arthritis, multiple sclerosis and posterior intraocular inflammation, uveitic disorders, ocular surface inflammatory disorders, neovascular disease, proliferative vitreoretinopathy, atherosclerosis, endometriosis, rheumatoid arthritis, hemangioma, diabetes mellitus, diabetic retinopathies, inflammatory bowel disease, Crohn's disease, psoriasis, Alzheimer's disease, lupus, vascular stenosis, restenosis, inflammatory joint disease, atherosclerosis, urinary obstructive syndromes, asthma, carcinoma, lymphoma, blastoma, sarcoma, and leukemia, lymphoid malignancies, squamous cell cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric cancer, stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney/renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, and head and neck cancer and other cancers. Other diseases or conditions include those caused by or mediated by or involving a virus or a parasite, such as, but not limited to, Myxoma virus, Vaccinia virus, Tanapox virus, Epstein-Barr virus, Herpes simplex

virus, Cytomegalovirus, Herpesvirus saimiri, Hepatitis B virus, African swine fever virus, Parovirus, Human Immune deficiency virus (HIV), Hepatitis C virus, Influenza virus, Respiratory syncytial virus, Measles virus, Vesicular stomatitis virus, Dengue virus and Ebola virus.

Also provided are combinations and kits containing the combinations, with optional instructions and/or reagents. These combinations contain compositions that contain two and one or more different cell surface receptor isoforms and/or a therapeutic drug or a cell surface receptor isoform and a therapeutic drug. The isoforms and/or drugs can be in separate compositions or in a single composition or one composition containing two or more of the agents and the other containing the other agents or other such formal. Methods of treatment by administering the components of the combination are provided. Each component can be administered separately, simultaneously, intermittently, in a single composition or combinations thereof.

BRIEF DESCRIPTION OF THE FIGURE

Figure 1 depicts angiogenic and endothelial cell maintenance pathways. Target points for CSR isoform modulation of one or more pathway steps are indicated. In particular, the figure depicts steps in the formation, maintenance and remodeling of the vasculature. These include the role(s) of VEGF's in recruitment of circulating endothelial precursors (CEPs), the roles of angioipoietin-2 in vessel destabilization.

DETAILED DESCRIPTION

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, 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 is 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 is understood that such identifiers can change and particular information on the internet can come and go, but equivalent information is known and

can be readily accessed, such as by searching the internet and/or appropriate databases. Reference thereto evidences the availability and public dissemination of such information.

As used herein, a cell surface receptor (CSR) is a protein that is expressed on the surface of a cell and typically includes a transmembrane domain or other moiety that anchors it to the surface of a cell. As a receptor it binds to ligands that mediate or participate in an activity of the cell surface receptor, such as signal transduction or ligand internalization. Cell surface receptors include, but are not limited to, single transmembrane receptors and G-protein coupled receptors. Receptor tyrosine kinases, such as growth factor receptors, also are among such cell surface receptors.

As used herein, a receptor tyrosine kinase (RTK) refers to a protein, typically a glycoprotein, that is a member of the growth factor receptor family of proteins. Growth factor receptors are typically involved in cellular processes including cell growth, cell division, differentiation, metabolism and cell migration. RTKs also are known to be involved in cell proliferation, differentiation and determination of cell fate as well as tumor growth. RTKs have a conserved domain structure including an extracellular domain, a membrane-spanning (transmembrane) domain and an intracellular tyrosine kinase domain. Typically, the extracellular domain binds to a polypeptide growth factor or a cell membrane-associated molecule or other ligand. The tyrosine kinase domain is involved in positive and negative regulation of the receptor.

Receptor tyrosine kinases are grouped into families based on, for example, structural arrangements of sequence motifs in their extracellular domains. Structural motifs include, but are not limited to repeats of regions of: immunoglobulin, fibronectin, cadherin, epidermal growth factor and kringle repeats. Classification by structural motifs has identified greater than 16 families of RTKs, each with a conserved tyrosine kinase domain. Examples of RTKs include, but are not limited to, erythropoietin-producing hepatocellular (EPH) receptors, epidermal growth factor (EGF) receptors, fibroblast growth factor (FGF) receptors, platelet-derived growth factor (PDGF) receptors, vascular endothelial growth factor (VEGF) receptor, cell adhesion RTKs (CAKs) , Tie/Tek receptors, insulin-like growth factor (IGF)

receptors, and insulin receptor related (IRR) receptors. Exemplary genes encoding RTKs include, but are not limited to, ErbB2, ErbB3, DDR1, DDR2, EGFR, EphA1, EphA8, FGFR-2, FGFR-4, Flt1 (fms-related tyrosine kinase 1 receptor; also known as VEGFR-1), FLK1 (also known as VEGFR-2), MET, PDGFR-A, PDGFR-B, and TEK (also known as TIE-2).

Dimerization of RTKs activates the catalytic tyrosine kinase domain of the receptor and tyrosine autophosphorylation. Autophosphorylation in the kinase domain maintains the tyrosine kinase domain in an activated state. Autophosphorylation in other regions of the protein influences interactions of the receptor with other cellular proteins. In some RTKs, ligand binding to the extracellular domain leads to dimerization of the receptor. In some RTKs, the receptor can dimerize in the absence of ligand. Dimerization also can be increased by receptor overexpression.

As used herein, a tumor necrosis factor receptor (TNFR) refers to a member of a family of receptors that have a characteristic repeating extracellular cysteine-rich motif such as found in TNFR1 and TNFR2. TNFRs also have a variable intracellular domain that differs between members of the TNFR family. The TNFR family of receptors includes, but is not limited to, TNFR1, TNFR2, TNFRrp, the low-affinity nerve growth factor receptor, Fas antigen, CD40, CD27, CD30, 4-1BB, OX40, DR3, DR4, DR5, and herpesvirus entry mediator (HVEM). Ligands for TNFRs include TNF- α, lymphotoxin, nerve growth factor, Fas ligand, CD40 ligand, CD27 ligand, CD30 ligand, 4-1BB ligand, OX40 ligand, APO3 ligand, TRAIL and LIGHT. TNFRs include an extracellular domain, including a ligand binding domain, a transmembrane domain and an intracellular domain that participates in signal transduction. TNFRs are typically trimeric proteins that trimerize at the cell surface.

As used herein, an isoform of a cell surface receptor (also referred to herein as a CSR isoform), such as an isoform of a receptor tyrosine kinase, refers to a receptor that lacks a domain or portion thereof sufficient to alter an activity of the receptor or modulate an activity compared to a wildtype and/or predominant form of the receptor or lacks a structural feature, such as a domain. Thus, a CSR isoform refers to a receptor that lacks a domain or portion of a domain sufficient to alter an activity, typically a biological activity, of the receptor. A CSR isoform lacks a domain or

portion of a domain sufficient to alter or modulate an activity of the receptor. A CSR isoform can include an isoform that has one or more biological activities that are altered from the receptor; for example, an isoform can include the alteration of the extracellular domain of p185-HER2, altering the isoform from a positively acting regulatory polypeptide of the receptor to a negatively acting regulatory polypeptide of the isoform, *e.g.* from a receptor domain into a ligand. Generally, an activity is altered in an isoform at least 0.1, 0.5, 1, 2, 3, 4, 5, or 10 fold compared to a wildtype and/or predominant form of the receptor. Typically, a activity is altered by at 2, 5, 10, 20, 50, 100 or 1000 fold or more. In one embodiment, alteration of an activity is a reduction in the activity. With reference to an isoform, alteration of activity refers to difference in activity between the particular isoform, which is shortened, compared to the unshortened form of the receptor. Alteration of an activity includes an enhancement or a reduction of activity. In one embodiment, an alteration of an activity is a reduction in biological activity; the reduction can be at least 0.1 0.5 1, 2, 3, 4, 5, or 10 fold compared to a wildtype and/or predominant form of the receptor. Typically, a biological activity is reduced 5, 10, 20, 50, 100 or 1000 fold or more.

As used herein, reference to modulating the activity of a cell surface receptor means that a CSR interacts in some manner with the receptor and activity, such as ligand binding or dimerization or other signal-transduction-related activity is altered.

As used herein, reference to a CSR isoform with altered activity refers to an alteration in an activity by virtue of the different structure or sequence of the CSR isoform compared to a cognate receptor.

As used herein, an intron fusion protein refers to an isoform that lacks one or more domain(s) or portion of one or more domain(s) resulting in an alteration of an activity of a receptor. The activity can be altered by the intron fusion protein directly, such as by interaction with the receptor, or indirectly by interacting with a receptor ligand or co-factor or other modulator of receptor activity. Intron fusion proteins isolated from cells or tissues or that have the sequence of such polypeptides isolated from cells or tissues, are "natural." Those that do not occur naturally but that are synthesized or prepared by linking a molecule to an intron such that the resulting

construct modulates the activity of a CSR are "synthetic." Included among intron fusion proteins are cell surface receptor isoforms that lack one or more domain(s) or portion of one or more domain(s) resulting in an alteration of an activity of a receptor. In addition, an intron fusion protein contains one or more amino acids not encoded by an exon (with reference to the predominant or wildtype form of a receptor), operatively linked to exon-encoded amino acids. Generally such isoforms are shortened compared to a wildtype or predominant form encoded by a CSR gene. They, however, can include insertions or other modifications in the exon portion and, thus, be of the same size or larger than the predominant form. Each, however, includes an intron-encoded portion (at least one amino acid, generally at least, 2, 3, 4, 5, 8, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75 and more amino acids). An intron fusion protein can be encoded by an alternatively spliced RNA and/or RNA molecules identified *in silico* by identifying potential splice sites and then producing such molecules by recombinant methods. Typically, an intron fusion protein is shortened by the presence of one or more stop codons in an intron fusion protein-encoding RNA that are not present in the corresponding sequence of an RNA encoding a wildtype or predominant form of a CSR polypeptide. Addition of amino acids and/or a stop codon can result in an intron fusion protein that differs in size and sequence from a wildtype or predominant form of a polypeptide.

Intron fusion proteins for purposes herein include natural combinatorial and synthetic intron fusion proteins. A natural intron fusion protein refers to a polypeptide that is encoded by an alternatively spliced RNA molecule that contains one or more amino acids encoded by an intron linked to one or more portions of the polypeptide encoded by one or more exons of a gene. Alternatively spliced mRNA is isolated or can be prepared synthetically by joining splice donor and acceptor sites in a gene. A natural intron fusion protein contains one or more amino acids and/or a stop codon encoded by an intron sequence and generally occurs in cells and/or tissues, but can be identified from a gene by identifying splice donor and acceptor sites and identifying possible encoded spliced variants. A combinatorial intron fusion protein refers to a polypeptide that is shortened compared to a wildtype or predominant form

of a polypeptide. Typically, the shortening removes one or more domains or a portion thereof from a polypeptide such that an activity is altered. Combinatorial intron fusion proteins often mimic a natural intron fusion protein in that one or more domains or a portion thereof that is/are deleted in a natural intron fusion protein derived from the same gene or derived from a gene in a related gene family. Those that do not occur naturally but that are synthesized or prepared by linking a molecule to an intron such that the resulting construct modulates the activity of a CSR are "synthetic."

As used herein, natural with reference to intron fusion protein, refers to any protein, polypeptide or peptide or fragment thereof (by virtue of the presence of the appropriate splice acceptor/donor sites) that is encoded within the genome of an animal and/or is produced or generated in an animal or that could be produced from a gene. Natural intron fusion proteins include allelic variants. Intron fusion proteins can be modified post-translationally.

As used herein, an exon refers to a nucleic acid molecule containing sequence of nucleotides that is transcribed into RNA and is represented in a mature form of RNA, such as mRNA (messenger RNA), after splicing and other RNA processing. An mRNA contains one or more exons operatively linked. Exons can encode polypeptides or a portion of a polypeptide. Exons also can contain non-translated sequences for example, translational regulatory sequences. Exon sequences are often conserved and exhibit homology among gene family members.

As used herein, an intron refers to a sequence of nucleotides that is transcribed into RNA and is then typically removed from the RNA by splicing to create a mature form of an RNA, for example, an mRNA. Typically, nucleotide sequences of introns are not incorporated into mature RNAs, nor are intron sequences or a portion thereof typically translated and incorporated into a polypeptide. Splice signal sequences such as splice donors and acceptors are used by the splicing machinery of a cell to remove introns from RNA. It is noteworthy that an intron in one splice variant can be an exon (i.e., present in the spliced transcript) in another variant. Hence, spliced mRNA encoding an intron fusion protein can include an exon(s) and introns.

As used herein, splicing refers to a process of RNA maturation where introns in the mRNA are removed and exons are operatively linked to create a messenger RNA (mRNA).

As used herein, alternative splicing refers to the process of producing multiple mRNAs from a gene. Alternate splicing can include operatively linking less than all the exons of a gene, and/or operatively linking one or more alternate exons that are not present in all transcripts derived from a gene.

As used herein, exon deletion refers to an event of alternative RNA splicing that produces a nucleic acid molecule that lacks at least one exon compared to an RNA molecule encoding a wildtype or predominant form of a polypeptide. An RNA molecule that has a deleted exon can be produced by such alternative splicing or by any other method, such as an *in vitro* method to delete the exon.

As used herein, exon insertion, refers to an event of alternative RNA splicing that produces a nucleic acid molecule that contains at least one exon not typically present in an RNA molecule encoding a wildtype or predominant form of a polypeptide. An RNA molecule that has an inserted exon can be produced by such alternative splicing or by any other method, such as an *in vitro* method to add or insert the exon.

As used herein, exon extension refers to an event of alternative RNA splicing that produces a nucleic acid molecule that contains at least one exon that is greater in length (number of nucleotides contained in the exon) than the corresponding exon in an RNA encoding a wildtype or predominant form of a polypeptide. An RNA molecule that has an extended exon can be produced by such alternative splicing or by any other method, such as an *in vitro* method to extend the exon. In some instances, as described herein, an mRNA produced by exon extension encodes an intron fusion protein.

As used herein, exon truncation refers to an event of alternative RNA splicing that produces a nucleic acid molecule that contains a truncation or shortening of one or more exons such that the one or more exons are shorter in length (number of nucleotides) compared to a corresponding exon in an RNA molecule encoding a wildtype or predominant form of a polypeptide. An RNA molecule that has a

truncated exon can be produced by such alternative splicing or by any other method, such as an *in vitro* method to truncate the exon.

As used herein intron retention refers to an event of alternative RNA splicing that produces a nucleic acid molecule that contains an intron or a portion thereof operatively linked to one or more exons. An RNA molecule that retains an intron or portion thereof can be produced by such alternative splicing or by any other method, such as *in vitro* method to produce an RNA molecule with a retained exon. In some cases, as described herein, an mRNA molecule produced by intron retention encodes an intron fusion protein.

As used herein, a gene, also referred to as a gene sequence, refers to a sequence of nucleotides transcribed into RNA (introns and exons), including nucleotide sequence that encodes at least one polypeptide. A gene includes sequences of nucleotides that regulate transcription and processing of RNA. A gene also includes regulatory sequences of nucleotides such as promoters and enhancers, and translation regulation sequences.

As used herein, a splice site refers to one or more nucleotides within the gene that participate in the removal of an intron and/or the joining of an exon. Splice sites include splice acceptor sites and splice donor sites.

As used herein, cognate receptor with reference to the isoforms provided herein refers to the receptor that is encoded by the same gene as the particular isoform. Generally, the cognate receptor also is a predominant form in a particular cell or tissue. For example, herstatin is encoded by a splice variant of the pre-mRNA which encodes p185-HER2 (ErbB2 receptor). Thus, p185-HER2 is the cognate receptor for herstatin.

As used herein, a wildtype form, for example, a wildtype form of a polypeptide, refers to a polypeptide that is encoded by a gene. Typically a wildtype form refers to a gene (or RNA or protein derived therefrom) without mutations or other modifications that alter function or structure; wildtype forms include allelic variation among and between species.

As used herein, a predominant form, for example, a predominant form of a polypeptide, refers to a polypeptide that is the major polypeptide produced from a

gene. A "predominant form" varies from source to source. For example, different cells or tissue types can produce different forms of polypeptides, for example, by alternative splicing and/or by alternative protein processing. In each cell or tissue type, a different polypeptide can be a "predominant form."

As used herein, a domain refers to a portion (typically a sequence of three or more, generally 5 or 7 or more amino acids) of a polypeptide chain that can form an independently folded structure within a protein made up of one or more structural motifs (e.g. combinations of alpha helices and/or beta strands connected by loop regions) and/or that is recognized by virtue of a functional activity, such as kinase activity. A protein can have one, or more than one, distinct domain. For example, a domain can be identified, defined or distinguished by homology of the sequence therein to related family members, such as homology and motifs that define an extracellular domain. In another example, a domain can be distinguished by its function, such as by enzymatic activity, *e.g.* kinase activity, or an ability to interact with a biomolecule, such as DNA binding, ligand binding, and dimerization. A domain independently can exhibit a biological function or activity such that the domain independently or fused to another molecule can perform an activity, such as, for example proteolytic activity or ligand binding. A domain can be a linear sequence of amino acids or a non-linear sequence of amino acids from the polypeptide. Many polypeptides contain a plurality of domains. For example, receptor tyrosine kinases typically include, an extracellular domain, a membrane-spanning (transmembrane) domain and an intracellular tyrosine kinase domain.

As used herein, a polypeptide lacking all or a portion of a domain refers a polypeptide that has a deletion of one or more amino acids or all of the amino acids of a domain compared to a cognate polypeptide. Amino acids deleted in a polypeptide lacking all or part of a domain need not be contiguous amino acids within the domain of the cognate polypeptide. Polypeptides that lack all or a part of a domain can include the loss or reduction of an activity of the polypeptide compared to the activity of a cognate polypeptide or loss of a structure in the polypeptide.

For example, if a cognate receptor has a transmembrane domain, then a receptor isoform polypeptide lacking all or a part of the transmembrane domain can

have a deletion of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 , 19, 20 or more amino acids between amino acids corresponding to the same amino acid positions in the cognate receptor.

As used herein, a polypeptide that contains a domain refers to a polypeptide that contains a complete domain with reference to the corresponding domain of a cognate receptor. A complete domain is determined with reference to the definition of that particular domain within a cognate polypeptide. For example, a receptor isoform comprising a domain refers to an isoform that contains a domain corresponding to the complete domain as found in the cognate receptor. If a cognate receptor, for example, contains a transmembrane domain of 21 amino acids between amino acid positions 400-420, then a receptor isoform that comprises such transmembrane domain, contains a 21 amino acid domain that has substantial identity with the 21 amino acid domain of the cognate receptor. Substantial identity refers to a domain that can contain allelic variation and conservative substitutions as compared to the domain of the cognate receptor. Domains that are substantially identical do not have deletions, non-conservative substitutions or insertions of amino acids compared to the domain of the cognate receptor. Domains (*i.e.*, a furin domain, an Ig-like domain) often are identified by virtue of structural and/or sequence homology to domains in particular proteins.

Such domains are known to those of skill in the art who can identify such. For exemplification herein, definitions are provided, but it is understood that it is well within the skill in the art to recognize particular domains by name. If needed appropriate software can be employed to identify domains.

As used herein, an extracellular domain is a portion of the cell surface receptor that occurs on the surface of the receptor and includes the ligand binding site(s). In one example, an ephrin receptor ligand binding domain (EPH_lbd) is the portion of the polypeptide that mediates binding of a protein receptor to an ephrin ligand. Typically, EphA receptors bind to GPI-anchored ephrin-A ligands, while EphB receptors bind to ephrin-B proteins that have a transmembrane and cytoplasmic domain.

A Receptor L domain (RLD), such as for example in ErbB2, is another example of a domain that includes a ligand binding site. Each L domain contains a single-stranded right hand beta-helix that can associate with a second L domain to form a three-dimensional bilobal structure surrounding a central space of sufficient size to accommodate a ligand molecule.

As used herein, a furin domain is a domain recognized as such by those of skill in the art and is a cysteine rich region. Furin is a type 1 transmembrane serine protease. A furin domain functions as a cleavage site for furin protease

As used herein a Sema domain is a domain recognized as such by those of skill in the art and is a receptor recognition and binding module. The Sema domain is characterized by a conserved set of cysteine residues, which form four disulfide bonds to stabilize the structure. The Sema domain fold is a variation of a β propeller topology, with seven blades radially arranged around a central axis. Each blade contains a four-stranded antiparallel β sheet. The Sema domain uses a 'loop and hook' system to close the circle between the first and the last blades. The blades are constructed sequentially with an N-terminal β-strand closing the circle by providing the outermost strand of the seventh (C-terminal) blade. The β-propeller is further stabilized by an extension of the N-terminus, providing an additional, fifth β-strand on the outer edge of blade 6.

As used herein, a plexin domain is a domain recognized as such by those of skill in the art and contains a cysteine rich repeat. Plexins are receptors that as a complex interact with membrane-bound semaphorins. The plexins contain three domains with homology to c-met, the receptor for scatter factor-induced motility, but they lack the intrinsic tyrosine kinase activity of c-met. Intracellullarly, invariant arginines identify a plexin domain with homology to guanosine triphosphatase-activating proteins. A protein can contain one, or more than one, plexin domain. As described herein, the MET receptor contains a single plexin domain.

As used herein, the F 5/8 type C domain is a domain recognized as such by those of skill in the art and is a domain that exhibits a distorted jelly-roll β-barrel motif, containing eight antiparallel strands arranged in two β-sheets. The lower part of the β-barrel is characterized by a preponderance of basic residues and three adjacent

protruding loops. The portion of the polypeptide that forms the F 5/8 type C domain contains two conserved cysteines, which link the extremities of the domain by a disulfide bond.

As used herein an Ig-like domain is a domain recognized as such by those of skill in the art and is a domain containing folds of beta strands forming a compact folded structure of two beta sheets stabilized by hydrophobic interactions and sandwiched together by an intra-chain disulfide bond. In one example, an Ig-like C-type domain contains seven beta strands arranged as four-strand plus three-strand so that four beta strands form one beta sheet and three beta strands form the second beta sheet. In another example, an Ig-like V-type domain contains nine beta strands arranged as four beta strands plus five beta strands (Janeway C.A. et al. (eds): Immunobiology-the immune system in health and disease, 5th edn. New York, Garland Publishing, 2001.).

As used herein, a fibronectin type-III (FN3) domain is a domain recognized as such by those of skill in the art and contains a conserved β sandwich fold with one β sheet containing four strands and the other sheet containing three strands. The folded structure of an FN3 domain and an Ig-like domain are topologically very similar except the FN3 domain lacks a conserved disulfide bond. The portion of the polypeptide encoding an FN3 domain also is characterized by a short stretch of amino acids containing an Arg–Gly–Asp (RGD) that mediates interactions with cell adhesion molecules to modulate thrombosis, inflammation, and tumor metastasis. In one example, EphA1 contains two FN3 domains.

As used herein, an IPT/TIG domain is a domain recognized as such by those of skill in the art and has an immunoglobulin fold-like domain. Proteins contain one, or more than one, IPT/TIG domain. IPT/TIG domains are found in plexins, transcription factors, and extracellular regions of receptor proteins, such as for example the cell surface receptors MET and RON as described herein, that appear to regulate cell proliferation and cellular adhesion (Johnson CA et al, Journal of Medical Genetics, 40:311-319, (2003)).

As used herein, an EGF domain is a domain recognized as such by those of skill in the art and contains a repeat pattern involving a number of conserved cysteine

residues which are important to the three-dimensional structure of the protein, and hence its recognition by receptors and other molecules. The EGF domain as described herein contains six cysteine residues which are involved in forming disulfide bonds. An EGF domain forms a two-stranded β sheet followed by a loop to a C-terminal short two-stranded sheet. Subdomains between the conserved cysteines vary in length. Repeats of EGF domains are typically found in the extracellular domain of membrane-bound proteins, such as for example in Tie-1 as described herein. A variation of the EGF domain is the laminin (Lam) EGF domain which, as described herein, has eight instead of six conserved cysteines and therefore is longer than the average EGF module and contains a further disulfide bond C-terminal of the EGF-like region.

As used herein, a C6 domain is a cysteine rich domain of typically about 110 to 160 amino acids in the N-terminal region of the polypeptide. It can be subdivided into four, or in some cases three or more, modules of about 40 residues containing 6 conserved cysteines that participate in intrachain disulfide bonds. A protein can have one, or more than one, C6 domain. As described herein, for example, TNFR2 contains three C6 domains.

As used herein, a transmembrane domain spans the plasma membrane anchoring the receptor and generally includes hydrophobic residues.

As used herein, a cytoplasmic domain is a domain that participates in signal transduction and occurs in the cytoplasmic portion of a transmembrane cell surface receptor. In one example, the cytoplasmic domain can include a protein kinase (PK) domain. A PK domain is recognized as such by those of skill in the art and is a domain that contains a conserved catalytic core. The conserved catalytic core is recognized to have a glycine-rich stretch of residues in the vicinity of a lysine residue in the N-terminal extremity of the domain, which has been shown to be involved in ATP binding, and an aspartic acid residue in the central part of the catalytic domain, which is important for the catalytic activity of the enzyme. Typically, the PK domain can be a serine/threonine protein kinase or a tyrosine protein kinase domain depending on the substrate specificity of the receptor domain such that, for example, a protein containing a tyrosine kinase domain phosphorylates substrate proteins on

tyrosine residues whereas, for example, a protein containing a serine/threonine protein kinase domain phosphorylates substrate proteins on serine or threonine residues.

As used herein, sterile α motif (SAM) domain is considered a protein-protein interaction module. A SAM domain is recognized as such by those of skill in the art and is a domain that spreads over typically about 70 residues to form an independently folded structure arranged in a small five-helix bundle with two large interfaces. In one example, such as for example in the SAM domain of EphB2, each of the interfaces is able to form dimers. The ability of the SAM domain to form homo- or hetero-oligomers creates a binding surface that mediates protein protein interactions.

As used herein, an allelic variant or allelic variation references to a polypeptide encoded by a gene that differs from a reference form of a gene (i.e. is encoded by an allele). 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 typically 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, modification 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.

As used herein, an open reading frame refers to a sequence of nucleotides that encodes a functional polypeptide or a portion thereof, typically at least about fifty amino acids. An open reading frame can encode a full-length polypeptide or a portion thereof. An open reading frame can be generated by operatively linking one or more

exons or an exon and intron, when the stop codon is in the intron and all or a portion of the intron is in a transcribed mRNA.

As used herein, a polypeptide refers to two or more amino acids covalently joined. The terms "polypeptide" and "protein" are used interchangeably herein.

As used herein, truncation or shortening with reference to the shortening of a nucleic acid molecule or protein, refers to a sequence of nucleotides or amino acids that is less than full-length compared to a wildtype or predominant form of the protein or nucleic acid molecule.

As used herein, a reference gene refers to a gene that can be used to map introns and exons within a gene. A reference gene can be genomic DNA or portion thereof, that can be compared with, for example, an expressed gene sequence, to map introns and exons in the gene. A reference gene also can be a gene encoding a wildtype or predominant form of a polypeptide.

As used herein, a family or related family of proteins or genes refers to a group of proteins or genes, respectively that have homology and/or structural similarity and/or functional similarity with each other.

As used herein, a premature stop codon is a stop codon occurring in the open reading frame of a sequence before the stop codon used to produce or create a full-length form of a protein, such as a wildtype or predominant form of a polypeptide. The occurrence of a premature stop codon can be the result of, for example, alternative splicing and mutation.

As used herein, an expressed gene sequence refers to any sequence of nucleotides transcribed or predicted to be transcribed from a gene. Expressed gene sequences include, but are not limited to, cDNAs, ESTs, and *in silico* predictions of expressed sequences, for example, based on splice site predictions and *in silico* generation of spliced sequences.

As used herein, an expressed sequence tag (EST) is a sequence of nucleotides generated from an expressed gene sequence. ESTs are generated by using a population of mRNA to produce cDNA. The cDNA molecules can be produced for example, by priming from the polyA tail present on mRNAs. cDNA molecules also can be produced by random priming using one or more oligonucleotides which prime

cDNA synthesis internally in mRNAs. The generated cDNA molecules are sequenced and the sequences are typically stored in a database. An example of an EST database is dbEST found online at ncbi.nlm.nih.gov/ dbEST. Each EST sequence is typically assigned a unique identifier and information such as the nucleotide sequence, length, tissue type where expressed, and other associated data is associated with the identifier.

As used herein, a kinase is a protein that is able to phosphorylate a molecule, typically a biomolecule, including macromolecules and small molecules. For example, the molecule can be a small molecule, or a protein. Phosphorylation includes auto-phosphorylation. Some kinases have constitutive kinase activity. Other kinases require activation. For example, many kinases that participate in signal transduction are phosphorylated. Phosphorylation activates their kinase activity on another biomolecule in a pathway. Some kinases are modulated by a change in protein structure and/or interaction with another molecule. For example, complexation of a protein or binding of a molecule to a kinase can activate or inhibit kinase activity.

As used herein, designated refers to the selection of a molecule or portion thereof as a point of reference or comparison. For example, a domain can be selected as a designated domain for the purpose of constructing polypeptides that are modified within the selected domain. In another example, an intron can be selected as a designated intron for the purpose of identifying RNA transcripts that include or exclude the selected intron.

As used herein, modulate and modulation refer to a change of an activity of a molecule, such as a protein. Exemplary activities include, but are not limited to, biological activities, such as signal transduction and protein phosphorylation. Modulation can include an increase in the activity (*i.e.*, up-regulation agonist activity) a decrease in activity (*i.e.*, down-regulation or inhibition) or any other alteration in an activity (such as periodicity, frequency, duration, kinetics). Modulation can be context dependent and typically modulation is compared to a designated state, for example, the wildtype protein, the protein in a constitutive state, or the protein as expressed in a designated cell type or condition.

As used herein, inhibit and inhibition refer to a reduction in an activity, such as a biological activity, relative to the uninhibited activity.

As used herein, a composition refers to any mixture. It can be a solution, a suspension, liquid, powder, a paste, aqueous, non-aqueous or any combination thereof.

As used herein, a combination refers to any association between or among two or more items. The combination can be two or more separate items, such as two compositions or two collections, can be a mixture thereof, such as a single mixture of the two or more items, or any variation thereof. The elements of a combination are generally functionally associated or related. A kit is a packaged combination that optionally includes instructions for use of the combination or elements thereof and/or optionally include other reagents and vessels and tools and devices employed in the methods for which the kits are intended.

As used herein, a pharmaceutical effect refers to an effect observed upon administration of an agent intended for treatment of a disease or disorder or for amelioration of the symptoms thereof.

As used herein, treatment means any manner in which the symptoms of a condition, disorder or disease or other indication, are ameliorated or otherwise beneficially altered.

As used herein therapeutic effect means an effect resulting from treatment of a subject that alters, typically improves or ameliorates the symptoms of a disease or condition or that cures a disease or condition. A therapeutically effective amount refers to the amount of a composition, molecule or compound which results in a therapeutic effect following administration to a subject.

As used herein, the term "subject" refers to animals, including mammals, such as human beings. As used herein, a patient refers to a human subject.

As used herein, an activity refers to a function or functioning or changes in or interactions of a biomolecule, such as polypeptide. Exemplary, but not limiting of such activities are: complexation, dimerization, multimerization, receptor-associated kinase activity or other enzymatic or catalytic activity, receptor-associated protease activity, phosphorylation, dephosphorylation, autophosphorylation, ability to form

complexes with other molecules, ligand binding, catalytic or enzymatic activity, activation including auto-activation and activation of other polypeptides, inhibition or modulation of another molecule's function, stimulation or inhibition of signal transduction and/or cellular responses such as cell proliferation, migration, differentiation, and growth, degradation, membrane localization, membrane binding, and oncogenesis. An activity can be assessed by assays described herein and by any suitable assays known to those of skill in the art, including, but not limited to *in vitro* assays, including cell-based assays, *in vivo* assays, including assays in animal models for particular diseases. Biological activities refer to activities exhibited *in vivo*. For purposes herein, biological activity refers to any of the activities exhibited by a polypeptide provided herein.

As used herein, angiogenic diseases (or angiogenesis-related diseases) are diseases in which the balance of angiogenesis is altered or the timing thereof is altered. Angiogenic diseases include those in which an alteration of angiogenesis, such as undesirable vascularization, occurs. Such diseases include, but are not limited to cell proliferative disorders, including cancers, diabetic retinopathies and other diabetic complications, inflammatory diseases, endometriosis and other diseases in which excessive vascularization is part of the disease process, including those noted above.

As used herein, complexation refers to the interaction of two or more molecules such as two molecules of a protein to form a complex. The interaction can be by noncovalent and/or covalent bonds and includes, but is not limited to, hydrophobic and electrostatic interactions, Van der Waals forces and hydrogen bonds. Generally, protein-protein interactions involve hydrophobic interactions and hydrogen bonds. Complexation can be influenced by environmental conditions such as temperature, pH, ionic strength and pressure, as well as protein concentrations.

As used herein, dimerization refers to the interaction of two molecules of the same type, such as two molecules of a receptor. Dimerization includes homodimerization where two identical molecules interact. Dimerization also includes heterodimerization of two different molecules, such as two subunits of a receptor and dimerization of two different receptor molecules. Typically, dimerization involves

two molecules that interact with each other through interaction of a dimerization domain contained in each molecule.

As used herein, a ligand antagonist refers to the activity of a CSR isoform that antagonizes an activity that results from ligand interaction with a CSR.

As used herein, *in silico* refers to research and experiments performed using a computer. *In silico* methods include, but are not limited to, molecular modeling studies, biomolecular docking experiments, and virtual representations of molecular structures and/or processes, such as molecular interactions.

As used herein, biological sample refers to any sample obtained from a living or viral source or other source of macromolecules and biomolecules, and includes any cell type or tissue of a subject from which nucleic acid or protein or other macromolecule can be obtained. The biological sample can be a sample obtained directly from a biological source or to sample that is processed For example, isolated nucleic acids that are amplified constitute a biological sample. Biological samples include, but are not limited to, body fluids, such as blood, plasma, serum, cerebrospinal fluid, synovial fluid, urine and sweat, tissue and organ samples from animals and plants and processed samples derived therefrom. Also included are soil and water samples and other environmental samples, viruses, bacteria, fungi algae, protozoa and components thereof.

As used herein, macromolecule refers to any molecule having a molecular weight from the hundreds up to the millions. Macromolecules include peptides, proteins, nucleotides, nucleic acids, and other such molecules that are generally synthesized by biological organisms, but can be prepared synthetically or using recombinant molecular biology methods.

As used herein, a biomolecule is any compound found in nature, or derivatives thereof. Exemplary biomolecules include but are not limited to: oligonucleotides, oligonucleosides, proteins, peptides, amino acids, peptide nucleic acids (PNAs), oligosaccharides and monosaccharides.

As used herein, the term "nucleic acid" refers to single-stranded and/or double-stranded polynucleotides such as deoxyribonucleic acid (DNA), and ribonucleic acid (RNA) as well as analogs or derivatives of either RNA or DNA.

Also included in the term "nucleic acid" are analogs of nucleic acids such as peptide nucleic acid (PNA), phosphorothioate DNA, and other such analogs and derivatives or combinations thereof. Nucleic acid can refer to polynucleotides such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The term also includes, as equivalents, derivatives, variants and analogs of either RNA or DNA made from nucleotide analogs, single (sense or antisense) and double-stranded polynucleotides. Deoxyribonucleotides include deoxyadenosine, deoxycytidine, deoxyguanosine and deoxythymidine. For RNA, the uracil base is uridine.

As used herein, the term "polynucleotide" refers to an oligomer or polymer containing at least two linked nucleotides or nucleotide derivatives, including a deoxyribonucleic acid (DNA), a ribonucleic acid (RNA), and a DNA or RNA derivative containing, for example, a nucleotide analog or a "backbone" bond other than a phosphodiester bond, for example, a phosphotriester bond, a phosphoramidate bond, a phophorothioate bond, a thioester bond, or a peptide bond (peptide nucleic acid). The term "oligonucleotide" also is used herein essentially synonymously with "polynucleotide," although those in the art recognize that oligonucleotides, for example, PCR primers, generally are less than about fifty to one hundred nucleotides in length.

Polynucleotides can include nucleotide analogs, for example, mass modified nucleotides, which allow for mass differentiation of polynucleotides; nucleotides containing a detectable label such as a fluorescent, radioactive, luminescent or chemiluminescent label, which allow for detection of a polynucleotide; or nucleotides containing a reactive group such as biotin or a thiol group, which facilitates immobilization of a polynucleotide to a solid support. A polynucleotide also can contain one or more backbone bonds that are selectively cleavable, for example, chemically, enzymatically or photolytically. For example, a polynucleotide can include one or more deoxyribonucleotides, followed by one or more ribonucleotides, which can be followed by one or more deoxyribonucleotides, such a sequence being cleavable at the ribonucleotide sequence by base hydrolysis. A polynucleotide also can contain one or more bonds that are relatively resistant to cleavage, for example, a chimeric oligonucleotide primer, which can include

nucleotides linked by peptide nucleic acid bonds and at least one nucleotide at the 3' end, which is linked by a phosphodiester bond or other suitable bond, and is capable of being extended by a polymerase. Peptide nucleic acid sequences can be prepared using well-known methods (see, for example, Weiler et al. Nucleic acids Res. 25: 2792-2799 (1997)).

As used herein, synthetic, in the context of a synthetic sequence and synthetic gene refers to a nucleic acid molecule that is produced by recombinant methods and/or by chemical synthesis methods.

As used herein, oligonucleotides refer to polymers that include DNA, RNA, nucleic acid analogues, such as PNA, and combinations thereof. For purposes herein, primers and probes are single-stranded oligonucleotides or are partially single-stranded oligonucleotides.

As used herein, primer refers to an oligonucleotide containing two or more deoxyribonucleotides or ribonucleotides, generally 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, production by recombinant means by using recombinant DNA methods means the use of the well-known methods of molecular biology for expressing proteins encoded by cloned DNA.

As used herein, "isolated," with reference to a molecule, such as a nucleic acid molecule, oligonucleotide, polypeptide or antibody, indicates that the molecule has been altered by the hand of man from how it is found in its natural environment. For example, a molecule produced by and/or contained within a recombinant host cell is considered "isolated." Likewise, a molecule that has been purified, partially or substantially, from a native source or recombinant host cell, or produced by synthetic methods, is considered "isolated." Depending on the intended application, an isolated molecule can be present in any form, such as in an animal, cell or extract thereof; dehydrated, in vapor, solution or suspension; or immobilized on a solid support.

As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is an episome, i.e., a nucleic acid capable of extra chromosomal replication. Vectors include those capable of autonomous replication and/or expression of nucleic acids to which they are linked. Vectors capable of directing the expression of genes to which they are operatively linked are referred to herein as "expression vectors." In general, expression vectors are often in the form of "plasmids," which are generally circular double stranded DNA loops that, in their vector form are not bound to the chromosome. "Plasmid" and "vector" are used interchangeably as the plasmid is the most commonly used form of vector. Other such other forms of expression vectors that serve equivalent functions and that become known in the art subsequently hereto.

As used herein, "transgenic animal" refers to any animal, generally a non-human animal, e.g., a mammal, bird or an amphibian, in which one or more of the cells of the animal contain heterologous nucleic acid introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. This molecule can be stably integrated within a chromosome, i.e., replicate as part of the chromosome, or it can be extrachromosomally replicating DNA. In the typical transgenic animals, the transgene causes cells to express a recombinant form of a protein.

As used herein, a reporter gene construct is a nucleic acid molecule that includes a nucleic acid encoding a reporter operatively linked to a transcriptional control sequences. Transcription of the reporter gene is controlled by these sequences. The activity of at least one or more of these control sequences is directly or indirectly regulated by another molecule such as a cell surface protein, a protein or small molecule involved in signal transduction within the cell. The transcriptional control sequences include the promoter and other regulatory regions, such as enhancer sequences, that modulate the activity of the promoter, or control sequences that modulate the activity or efficiency of the RNA polymerase. Such sequences are herein collectively referred to as transcriptional control elements or sequences. In addition,

the construct can include sequences of nucleotides that alter translation of the resulting mRNA, thereby altering the amount of reporter gene product.

As used herein, "reporter" or "reporter moiety" refers to any moiety that allows for the detection of a molecule of interest, such as a protein expressed by a cell, or a biological particle. Typical reporter moieties include, for example, fluorescent proteins, such as red, blue and green fluorescent proteins (see, *e.g.*, U.S. Patent No. 6,232,107, which provides GFPs from *Renilla* species and other species), the lacZ gene from *E. coli*, alkaline phosphatase, chloramphenicol acetyl transferase (CAT) and other such well-known genes. For expression in cells, nucleic acid encoding the reporter moiety, referred to herein as a "reporter gene," can be expressed as a fusion protein with a protein of interest or under to the control of a promoter of interest.

As used herein, the phrase "operatively linked" with reference to sequences of nucleic acids means the nucleic acid molecules or segments thereof are covalently joined into one piece of nucleic acid such as DNA or RNA, whether in single or double stranded form. The segments are not necessarily contiguous, rather two or more components are juxtaposed so that the components are in a relationship permitting them to function in their intended manner. For example, segments of RNA (exons) can be operatively linked such as by splicing, to form a single RNA molecule. In another example, DNA segments can be operatively linked, whereby control or regulatory sequences on one segment control permit expression or replication or other such control of other segments. Thus, in the case of a regulatory region operatively linked to a reporter or any other polynucleotide, or a reporter or any polynucleotide operatively linked to a regulatory region, expression of the polynucleotide/reporter is influenced or controlled (*e.g.*, modulated or altered, such as increased or decreased) by the regulatory region. For gene expression, a sequence of nucleotides and a regulatory sequence(s) are connected in such a way to control or permit gene expression when the appropriate molecular signal, such as transcriptional activator proteins, are bound to the regulatory sequence(s). Operative linkage of heterologous nucleic acid, such as DNA, to regulatory and effector sequences of nucleotides, such as promoters, enhancers, transcriptional and translational stop sites, and other signal

sequences, refers to the relationship between such DNA and such sequences of nucleotides. For example, operative linkage of heterologous DNA to a promoter refers to the physical relationship between the DNA and the promoter such that the transcription of such DNA is initiated from the promoter by an RNA polymerase that specifically recognizes, binds to and transcribes the DNA in reading frame.

As used herein, the term "operatively linked" with reference to amino acids in polypeptides refers to covalent linkage (direct or indirect) of the amino acids. For example, when used in the context of the phrase "at least one domain of a cell surface receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding a cell surface receptor", means that the amino acids of a domain from a cell surface receptor are covalently joined to amino acids encoded by an intron from a cell surface receptor gene such as by linkage, typically direct linkage via peptide bonds, or the linkage also can be effected indirectly, such as via a linker or via non-peptidic linkage. Hence, a polypeptide that contains at least one domain of a cell surface receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding a cell surface receptor can be an intron fusion protein. It contains one or more amino acids that are not found in a predominant form of the receptor but rather contains a portion that is encoded by an intron of the gene that encodes the predominant form. These one or more amino acids are encoded by an intron sequence of the gene encoding the cell surface receptor. Nucleic acids encoding such polypeptides can be produced when an intron sequence is spliced or otherwise covalently joined in-frame to an exon sequence that encodes a domain of a cell surface receptor. Translation of the nucleic acid molecule produces a polypeptide where the amino acid(s) of the intron sequence are covalently joined to a domain of the cell surface receptor. They also can be produced synthetically by linking a portion containing an exon to a portion containing an intron, including chimeric intron fusion proteins in which the exon is encoded by a gene for a different cell surface receptor isoform from the intron portion.

As used herein, the phrase "generated from a nucleic acid" in reference to the generating of a polypeptide, such as an isoform and intron fusion protein, includes the literal generation of a polypeptide molecule and the generation of an amino acid

sequence of a polypeptide from translation of the nucleic acid sequence into a sequence of amino acids.

As used herein, a promoter region refers to the portion of DNA of a gene that controls transcription of the DNA to which it is operatively linked. The promoter region includes specific sequences of DNA that are sufficient for RNA polymerase recognition, binding and transcription initiation. This portion of the promoter region is referred to as the promoter. In addition, the promoter region includes sequences that modulate this recognition, binding and transcription initiation activity of the RNA polymerase. These sequences can be cis acting or can be responsive to trans acting factors. Promoters, depending upon the nature of the regulation, can be constitutive or regulated.

As used herein, regulatory region means a cis-acting nucleotide sequence that influences expression, positively or negatively, of an operatively linked gene. Regulatory regions include sequences of nucleotides that confer inducible (i.e., require a substance or stimulus for increased transcription) expression of a gene. When an inducer is present or at increased concentration, gene expression can be increased. Regulatory regions also include sequences that confer repression of gene expression (*i.e.*, a substance or stimulus decreases transcription). When a repressor is present or at increased concentration gene expression can be decreased. Regulatory regions are known to influence, modulate or control many *in vivo* biological activities including cell proliferation, cell growth and death, cell differentiation and immune modulation. Regulatory regions typically bind to one or more trans-acting proteins, which results in either increased or decreased transcription of the gene.

Particular examples of gene regulatory regions are promoters and enhancers. Promoters are sequences located around the transcription or translation start site, typically positioned 5' of the translation start site. Promoters usually are located within 1 Kb of the translation start site, but can be located further away, for example, 2 Kb, 3 Kb, 4 Kb, 5 Kb or more, up to and including 10 Kb. Enhancers are known to influence gene expression when positioned 5' or 3' of the gene, or when positioned in or a part of an exon or an intron. Enhancers also can function at a significant distance

from the gene, for example, at a distance from about 3 Kb, 5 Kb, 7 Kb, 10 Kb, 15 Kb or more.

Regulatory regions also include, in addition to promoter regions, sequences that facilitate translation, splicing signals for introns, maintenance of the correct reading frame of the gene to permit in-frame translation of mRNA, stop codons, leader sequences and fusion partner sequences, internal ribosome binding sites (IRES), elements for the creation of multigene or polycistronic messages, polyadenylation signals to provide proper polyadenylation of the transcript of a gene of interest and stop codons and can be optionally included in an expression vector.

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 generally in the "L" isomeric form. Residues in the "D" isomeric form can be substituted for any L-amino acid residue, as long as the desired functional property is retained by the polypeptide. NH2 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., 243:3552-59 (1969) and adopted at 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

All sequences of amino acid residues represented herein by a formula have a left to right orientation in the conventional direction of amino-terminus to carboxyl-terminus. In addition, the phrase "amino acid residue" is defined to include the amino acids listed in the Table of Correspondence modified, non-natural and unusual amino acids. 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 or to an amino-terminal group such as NH_2 or to a carboxyl-terminal group such as COOH.

In a peptide or protein, suitable conservative substitutions of amino acids are known to those of skill in this art and generally can be made without altering a biological activity of a 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).

Such substitutions may be made in accordance with those set forth in TABLE 2 as follows:

TABLE 2

Original residue	**Conservative substitution**
Ala (A)	Gly; Ser
Arg (R)	Lys
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
Phe (F)	Met; Leu; Tyr
Ser (S)	Thr
Thr (T)	Ser
Trp (W)	Tyr
Tyr (Y)	Trp; Phe
Val (V)	Ile; Leu

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

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 bioisoteres are peptidomimetics.

As used herein, "similarity" between two proteins or nucleic acids refers to the relatedness between the amino acid sequences 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 (Carillo, H. & Lipton, D., *SIAM J Applied Math 48*:1073 (1988)).

As used herein, sequence identity compared along the full length of a polypeptide compared to another polypeptide refers to the percentage of identity of an amino acid in a polypeptide along its full-length. For example, if a polypeptide A has 100 amino acids and polypeptide B has 95 amino acids, identical to amino acids 1-95 of polypeptide A, then polypeptide B has 95% identity when sequence identity is compared along the full length of a polypeptide A compared to full length of polypeptide B. As discussed below, and known to those of skill in the art, various programs and methods for assessing identity are known to those of skill in the art. High levels of identity, such as 90% or 95% identity, readily can be determined without software.

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; Carillo *et al.* (1988) *SIAM J Applied Math 48*:1073). By sequence homology, the number of conserved amino acids is determined by standard alignment algorithms 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 nucleic acid molecules have nucleotide 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 "FAST A" 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 (Atschul, S.F., *et al., J Molec Biol 215*:403 (1990); Guide to Huge Computers, Martin J. Bishop, ed., Academic Press, San Diego, 1994, and Carillo *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, 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 sequences. 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 an amino acid sequence 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, 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, unit dose form refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art.

B. Cell Surface Receptor (CSR) Isoforms

Provided herein are cell surface receptor (CSR) isoforms, families of CSR isoforms and methods of preparing CSR isoforms. The CSR isoforms differ from the cognate receptors in that there are insertions and/or deletions and the resulting CSR isoforms exhibit a difference in one or more activities or functions compared to the cognate receptor. Such changes include a change in a biological activity, such as elimination of kinase activity, and/or elimination of all or part of a transmembrane domain. The CSR isoforms provided herein can be used for modulating the activity of a cell surface receptor. They also can be used as targeting agents for delivery of molecules, such as drugs or toxins or nucleic acids, to targeted cells or tissues.

CSR isoforms can contain a new domain and/or exhibit a new or different biological function compared to a wildtype and/or predominant form of the receptor.

For example, intron-encoded amino acids can introduce a new domain or portion thereof into an isoform. Biological activities that can be altered include, but are not limited to, protein-protein interactions such as dimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, enzymatic activity such as kinase activity, response to regulatory molecules including regulatory proteins, cofactors, and other signaling molecules, such as in a signal transduction pathway.

Generally, a biological activity is altered in an isoform at least 0.1, 0.5, 1, 2, 3, 4, 5, or 10 fold compared to a wildtype and/or predominant form of the receptor. Typically, a biological activity is altered 10, 20, 50, 100 or 1000 fold or more. For example, an isoform can be reduced in a biological activity.

CSR isoforms also can modulate an activity of a wildtype and/or predominant form of the receptor. For example, a CSR isoform can interact directly or indirectly with a CSR isoform and modulate a biological activity of the receptor. Biological activities that can be altered include, but are not limited to, protein-protein interactions such as dimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, enzymatic activity such as kinase activity, response to regulatory molecules including regulatory proteins, cofactors, and other signaling molecules, such as in a signal transduction pathway.

A CSR isoform can interact directly or indirectly with a cell surface receptor to cause or participate in a biological effect, such as by modulating a biological activity of the cell surface receptor. A CSR isoform also can interact independently of a cell surface receptor to cause a biological effect, such as by initiating or inhibiting a signal transduction pathway. For example, a CSR isoform can initiate a signal transduction pathway and enhance or promote cell growth. In another example, a CSR isoform can interact with the cell surface receptor as a ligand causing a biological effect for example by inhibiting a signal transduction pathway that can impede or inhibit cell growth. Hence, the isoforms provided herein can function as cell surface receptor ligands in that they interact with the targeted receptor in the same manner that a cognate ligand interacts with and alters receptor activity. The isoforms

can bind as a ligand, but not necessarily, to a ligand binding site and serve to block receptor dimerization. They act as ligands in that they interact with the receptor. The CSR isoforms also can act by binding to ligands for the receptor and/or by preventing receptor activities, such as dimerization.

For example, a CSR isoform can compete with a CSR for ligand binding. A CSR isoform, when it binds to receptor, can be a negative effector ligand, which results in inhibition of receptor function. It also is possible that some CSR isoforms bind a cognate receptor, resulting in activation of the receptor. A CSR isoform can act as a competitive inhibitor of a CSR, for example, by complexing with a CSR isoform and altering the ability of the CSR to multimerize (*e.g.* dimerize or trimerize) with other CSRs. A CSR isoform can compete with a CSR for interactions with other polypeptides and cofactors in a signal transduction pathway. The cell surface isoforms and families of isoforms provided herein include, but are not limited to, isoforms of receptor tyrosine kinases (also referred to herein as RTK isoforms) and isoforms of other families of CSRs, such as TNFs and other G-protein-coupled receptors. In one example, a CSR isoform is a soluble polypeptide. For example, a CSR isoform lacks at least part or all of a transmembrane domain. Soluble isoforms can modulate a biological activity of a wildtype or predominant form of a receptor (see for example, Kendall *et al.* (1993) PNAS 90: 10705, Werner *et al.* (1992) Molec. Cell Biol. 12: 82, Heaney *et al.* (1995) PNAS 92: 2365, Fukunaga *et al.* (1990) PNAS 87:8702, Wypych *et al.* (1995) Blood 85: 66-73, Barron *et al.* (1994) Gene 147:263, Cheng *et al.* (1994) Science 263: 1759, Dastot *et al.* (1996) PNAS 93:10723, Abramovich *et al.* (1994) FEBS Lett 338:295, Diamant *et al.* (1997) FEBS Lett 412:379, Ku *et al.* (1996) Blood 88:4124, Heaney ML and Golde DW (1998), J Leukocyte Biol. 64:135-146).

A cell surface receptor isoform can be produced by any method known in the art including isolation of isoforms expressed 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. Isoforms of cell surface receptors, including isoforms of receptor tyrosine kinases, can be encoded by alternatively spliced RNA molecules transcribed from a receptor tyrosine kinase gene. Such

isoforms include exon deletion, exon extension, exon truncation and intron retention alternatively spliced RNAs. CSR isoforms, include receptor isoforms that contain sequences encoded by introns (or alternative exons); also referred to as intron fusion proteins.

Pharmaceutical compositions containing one or more different CSR isoforms are provided. Also provided are methods of treatment of diseases and conditions by administering the pharmaceutical compositions or delivering a CSR isoform, such by administering a vector that encodes the isoform. Administration can be effected *in vivo* or *ex vivo*.

Methods of identifying and producing CSR isoforms and nucleic acid molecules encoding CSR isoforms are provided herein. Also provided are methods for expressing, isolating and formulating CSR isoforms.

Classes of CSR Isoforms

As noted, CSR isoforms are polypeptides that lack a domain or portion of a domain sufficient to remove or reduce or otherwise alter, including having a positive or negative effect, on biological activity compared to the cognate unbound form of the receptor. Some CSR isoforms also have completely novel functions as a result of the gain or loss of domains, or even single amino acid replacements. CSR isoforms represent splice variants of a gene (or recombinant shortened variants) and can be generated by alternate splicing or by recombinant or synthetic methods. CSR isoforms can be encoded by alternatively spliced RNAs. CSR isoforms also can be generated by recombinant methods and by use of *in silico* and synthetic methods.

Typically, a CSR isoform produced from an alternatively spliced RNA is not a predominant form of a polypeptide encoded by a gene. In some instances, a CSR isoform can be a tissue-specific or developmental stage-specific polypeptide or disease specific (*i.e.*, can be expressed at a difference level from tissue-to-tissue or stage-to-stage or in a disease state compared to a non-diseased state or only may be expressed in the tissue, at the stage or during the disease process or progress). Alternatively spliced RNA forms that can encode CSR isoforms include, but are not limited to, exon deletion, exon retention, exon extension, exon truncation, and intron

retention alternatively spliced RNAs. Included among CSR isoforms are intron fusion proteins.

(a) Alternative Splicing and Generation of CSR Isoforms

Genes in eukaryotes include introns and exons that are transcribed by RNA polymerase into RNA products generally referred to as pre-mRNA. Pre-mRNAs are typically intermediate products that are further processed through RNA splicing and processing to generate a final messenger RNA (mRNA). Typically, a final mRNA contains exons sequences and is obtained by splicing out the introns. Boundaries of introns and exons are marked by splice junctions, sequences of nucleotides that are used by the splicing machinery of the cell as signals and substrates for removing introns and joining together exon sequences. Exons are operatively linked together to form a mature RNA molecule. Typically, one or more exons in an mRNA contains an open reading frame encoding a polypeptide. In many cases, an open reading frame can be generated by operatively linking two or more exons; for example, a coding sequence can span exon junctions and an open reading frame is maintained across the junctions.

RNA also can undergo alternative splicing to produce a variety of different mRNA transcripts from a single gene. Alternatively spliced mRNAs can contain different numbers of and/or arrangements of exons. For example, a gene that has 10 exons can generate a variety of alternatively spliced mRNAs. Some mRNAs can contain all 10 exons, some with only 9, 8, 7, 6, 5 etc. In addition, products, for example, with 9 of the 10 exons, can be among a variety of mRNAs, each with a different exon missing. Alternatively spliced mRNAs can contain additional exons, not typically present in an RNA encoding a predominant or wild type form. Addition and deletion of exons includes addition and deletion, respectively of a 5' exon, 3'exon and an exon internal in an RNA. Alternatively spliced RNA molecules also include addition of an intron or a portion of an intron operatively linked to or within an RNA. For example, an intron normally removed by splicing in an RNA encoding a wildtype or predominant form can be present in an alternatively spliced RNA. An intron or intron portion can be operatively linked within an RNA, such as between two exons. An intron or intron portion can be operatively linked at one end of an RNA, such as at

the 3' end of a transcript. In some examples, the presence of intron sequence within an RNA terminates transcription based on poly-adenylation sequences within an intron.

Alternative RNA splicing patterns can vary depending upon the cell and tissue type. Alternative RNA splicing also can be regulated by developmental stage of an organism, cell or tissue type. For example, RNA splicing enzymes and polypeptides that regulate RNA splicing can be present at different concentrations in particular cell and tissue types and at particular stages of development. In some cases, a particular enzyme or regulatory polypeptide can be absent from a particular cell or tissue type or at particular stage of development. These differences can produce different splicing patterns for an RNA within a cell or tissue type or stage, thus giving rise to different populations of mRNAs. Such complexity can generate a number of protein products appropriate for particular cell types or developmental stages.

Alternatively spliced mRNAs can generate a variety of different polypeptides, also referred to herein as isoforms. Such isoforms can include polypeptides with deletions, additions and shortenings. For example, a portion of an open reading frame normally encoded by an exon can be removed in an alternatively spliced mRNA, thus resulting in a shorter polypeptide. An isoform can have amino acids removed at the N or C terminus or the deletion can be internal. An isoform can be missing a domain or a portion of a domain as a result of a deleted exon. Alternatively spliced mRNAs also can generate polypeptides with additional sequences. For example, a stop codon can be contained in an exon; when this exon is not included in an mRNA, the stop codon is not present and the open reading frame continues into the sequences contained in downstream exons. In such examples, additional open reading frame sequences add additional amino acid sequences to a polypeptide and can include addition of a new domain or a portion thereof.

(b) Intron Fusion Proteins

One class of isoforms is intron fusion proteins. An intron fusion protein is an isoform that lacks a domain or portion of a domain sufficient to remove or reduce a biological activity of a receptor. In addition, an intron fusion protein contains one or more amino acids not encoded by an exon, operatively linked to exon-encoded amino

acids and/or is shortened compared to a wildtype or predominant form encoded by a CSR gene. Typically, an intron fusion protein is shortened by the presence of one or more stop codons in an intron fusion protein-encoding RNA that are not present in the corresponding sequence of an RNA encoding a wildtype or predominant form of a CSR polypeptide. Addition of amino acids and/or a stop codon can result in an intron fusion protein that differs in size and sequence from a wildtype or predominant form of a polypeptide.

An intron fusion protein is modified in one or more biological activities. For example, addition of amino acids in an intron fusion protein can add, extend or modify a biological activity compared to a wildtype or predominant form of a polypeptide. For example, fusion of an intron encoded amino acid sequence to a protein can result in the addition of a domain with new functionality. Fusion of an intron encoded amino acid sequence to a protein also can modulate an existing biological activity of a protein, such as by inhibiting a biological activity, for example, inhibition of dimerization or inhibition of kinase activity.

Intron fusion proteins include natural and combinatorial intron fusion proteins. A natural intron fusion protein is encoded by an alternatively spliced RNA that contains one or more introns or a portion thereof operatively linked to one or more exons of a gene. A natural intron fusion protein contains one or more amino acids encoded by an intron sequence and/or an intron fusion protein can be shortened as a result of one or more stop codons encoded by an intron sequence operatively linked to one or more exons. A combinatorial intron fusion protein is a polypeptide that is shortened compared to a wildtype or predominant form of a polypeptide. Typically, the shortening removes one or more domains or a portion thereof from a polypeptide. Combinatorial intron fusion proteins often mimic a natural intron fusion protein in that one or more domains or a portion thereof is/are deleted as in a natural intron fusion protein derived from the same gene sequence or derived from a gene sequence in a related gene family.

i. Natural intron fusion proteins

Natural intron fusion proteins are generated from a class of alternatively spliced mRNAs that includes mRNAs that have incorporated intron sequences into

mRNA as well as exon sequences, such as intron retention RNA molecules and some exon extension RNAs. They include all such variants that occur and can be isolated from a cell or tissue, identified in a database or synthesized based upon the sequence and structure of a gene. Any splice variant that is possible and that includes one or more codons (including only a stop codon) from an intron is considered a natural intron fusion protein.

The incorporated intron sequences can include one or more introns or a portion thereof. Such mRNAs can arise by a mechanism of intron retention. For example, a pre-mRNA is exported from the nucleus to the cytoplasm of the cell before the splicing machinery has removed one or more introns. In some cases, splice sites can be actively blocked, for example by cellular proteins, preventing splicing of one or more introns.

Retention of one or more introns or a portion thereof also can lead to the generation of isoforms referred to herein as natural intron fusion proteins. For example, an intron sequence can contain an open reading frame that is operatively linked to the exon sequences by RNA splicing. Intron-encoded sequences can add amino acids to a polypeptide, for example, at either the N or C terminus of a polypeptide, or internally within a polypeptide. In some examples, an intron sequence also can contain one or more stop codons. An intron encoded stop codon that is operatively linked with an open reading frame in one or more exons can terminate the encoded polypeptide. Thus, an isoform can be produced that is shortened as a result of the stop codon. In some examples, an intron retained in an mRNA can result in the addition of one or more amino acids and a stop codon to an open reading frame, thereby producing an isoform that terminates with an intron encoded sequence.

Provided herein are natural intron fusion proteins, that can be generated by intron retention, including intron fusion proteins with addition of domains or portion of domains encoded by an intron and intron fusion proteins with one or more domains or portion of domain deleted. For example, an intron sequence can be operatively linked in place of an exon sequence that is typically within an mRNA for a gene. A domain or portion thereof encoded by the exon is thus deleted from and intron encoded amino acids are included in the encoded polypeptide.

In another example, an intron sequence is operatively linked in addition to the typically present exons in an mRNA. In one example, an operatively linked intron sequence can introduce a stop codon in-frame with exon sequences encoding a polypeptide. In another example, an operatively linked intron sequence can introduce one or more amino acids into a polypeptide. In some embodiments, a stop codon in-frame also is operatively linked with exon sequences encoding a polypeptide, thereby generating an mRNA encoding a polypeptide with intron-encoded amino acids at the C terminus.

In one example of a natural intron fusion protein, one or more amino acids encoded by an intron sequence are operatively linked at the C terminus of a polypeptide. For example, an intron fusion protein is generated from a nucleic acid sequence that contains one or more exon sequences at the 5' end of an RNA followed by one or more intron sequences or a portion of an intron sequence retained at the 3' end of an RNA. An intron fusion protein produced from such nucleic acid contains exon-encoded amino acids at the N-terminus and one or more amino acids encoded by an intron sequence at the C-terminus. In another example, an intron fusion protein is generated from a nucleic acid by operatively linking a stop codon encoded within an intron sequence to one or more exon sequences, thereby generating a nucleic acid sequence encoding shortened polypeptide.

ii. Combinatorial Intron fusion proteins

Intron fusion proteins also can be generated by recombinant methods and/or *in silico* and synthetic methods to produce polypeptides that are modified compared to a wildtype or predominant form of a polypeptide. Typically, combinatorial intron fusion proteins are shortened polypeptides compared to a wildtype or predominant form. Shortening can remove one or more domains or a portion thereof.

Combinatorial intron fusion proteins are mimics of so-called natural intron fusion proteins in that one or more domains or a portion thereof that are deleted in a natural intron fusion protein derived from the same gene sequence or derived from a gene sequence in a related gene family is/are deleted. For example, as is described further herein, by aligning sequences of gene family members, intron and exons, structures and encoded protein domains can be identified in the nucleic acid.

Recombinant nucleic acid molecules encoding polypeptides can be synthesized that contain one or more exons and an intron or portion thereof. Such recombinant molecules can contain one or more amino acids and/or a stop codon encoded by an intron, operatively linked to an exon, producing an intron fusion protein. Recombinant polypeptides also can be produced that contain a combinatorial intron fusion protein. As part of this method, potential immunogenic epitopes can be recognized using motif scanning, and modified with conservative amino acid substitutions or by other modifications well known in the art, such as PEGylation. Generally, any therapeutic intron fusion protein can be modified in this same way to achieve optimized pharmacokinetics or avoid immunogenicity.

(c) Intron-encoded isoforms

Another CSR isoform is an intron-encoded isoform. An intron-encoded isoform contains an intron sequences or portions thereof from an isoform, such as a natural intron fusion protein. An intron-encoded isoform can interact with a wildtype form or predominant form of a polypeptide produced from the same gene as the intron-encoded isoform. An intron-encoded isoforms can interact with a molecule in a signal transduction pathway that interact with a wildtype form or predominant form of a polypeptide produced from the same gene as the intron-encoded isoform. An intron-encoded isoform can be expressed or produced as a fusion with exon-encoded sequences. An intron-encoded isoform can be expressed or produced as a fusion with heterologous sequences such as a starting methionine. Stop codons can be engineered in the encoding nucleic acid molecule to terminate an intron-encoded isoform within or at the end of the intron sequence.

(d) Isoforms generated by exon modifications

CSR isoforms can be generated by modification of an exon relative to a corresponding exon of an RNA encoding a wildtype or predominant form of a CSR polypeptide. Exon modifications include alternatively spliced RNA forms such as exon truncations, exon extensions, exon deletions and exon insertions. These alternatively spliced RNA molecules can encode CSR isoforms which differ from a wildtype or predominant form of a CSR polypeptide by including additional amino

acids and/or by lacking amino acid sequences present in a wildtype or predominant form of a CSR polypeptide.

Exon insertions are alternative spliced RNA molecules that contains at least one exon not typically present in an RNA encoding a wildtype or predominant form of a polypeptide. An inserted exon can operatively link additional amino acids encoded by the inserted exon to the other exons present in an RNA. An inserted exon also can contain one or more stop codons such that the RNA encoded polypeptide terminates as a result of such stop codons. If an exon containing such stop codons is inserted upstream of an exon that contains the stop codon used for polypeptide termination of a wildtype or predominant form of a polypeptide, a shortened polypeptide can be produced.

An inserted exon can maintain an open reading frame, such that when the exon is inserted, the RNA encodes an isoform containing an amino acid sequence of a wildtype or predominant form of a polypeptide with additional amino acids encoded by the inserted exon. An inserted exon can be inserted 5', 3' or internally in an RNA, such that additional amino acids encoded by the inserted exon are linked at the N terminus, C-terminus or internally, respectively in an isoform. An inserted exon also can change the reading frame of an RNA in which it is inserted, such that an isoform is produced that contains only a portion of the sequence of amino acids in a wildtype or predominant form of a polypeptide. Such isoforms can additionally contain amino acid sequence encoded by the inserted exon and also can terminate as a result of a stop codon contained in the inserted exon.

CSR isoforms also can be produced from exon deletion events. An exon deletion refers to an event of alternative RNA splicing that produces a nucleic acid molecule that lacks at least one exon compared to an RNA encoding a wildtype or predominant form of a polypeptide. Deletion of an exon can produce a polypeptide of alternate size such as by removing sequences that encode amino acids as well as by changing the reading frame of an RNA encoding a polypeptide. An exon deletion can remove one or more amino acids from an encoded polypeptide; such amino acids can be N-terminal, C-terminal or internal to a polypeptide depending upon the location of the exon in an RNA sequence. Deletion of an exon in an RNA also can cause a shift

in reading frame such that an isoform is produced containing one or more amino acids not present in a wildtype or predominant form of a polypeptide. A shift in reading frame also can result in a stop codon in the reading frame producing an isoform that terminates at a sequence different from that of a wildtype or predominant form of a polypeptide. In one example, a shift of reading frame produces an isoform that is shortened compared to a wildtype or predominant form of a polypeptide. Such shortened isoforms also can contain sequences of amino acids not present in a wildtype or predominant form of a polypeptide.

CSR isoforms also can be produced by exon extension in an RNA. Exon extension is an event of alternative RNA splicing that produces a nucleic acid molecule that contains at least one exon that is greater in length (number of nucleotides contained in the exon) than the corresponding exon in an RNA encoding a wildtype or predominant form of a polypeptide. Additional sequence contained in an exon extension can encode additional amino acids and/or can contain a stop codon that terminates a polypeptide. An exon insertion containing an in-frame stop codon can produce a shortened isoform, that terminates in the sequence of the exon extension. An exon insertion also can shift the reading frame of an RNA, resulting in an isoform containing one or more amino acids not present in a wildtype or predominant form of a polypeptide and/or an isoform that terminates at a sequence different from that of a wildtype or predominant form of a polypeptide. An exon extension can include sequences contained in an intron of an RNA encoding a wildtype or predominant form of a polypeptide and thereby produce an intron fusion protein.

CSR isoforms also can be produced by exon truncation. Exon truncations are RNA molecules that contain a shortening of one or more exons such that the one or more exons are shorter in length (number of nucleotides) compared to a corresponding exon in an RNA encoding a wildtype or predominant form of a polypeptide. An RNA molecule with an exon truncation can produce a polypeptide that is shortened compared to a wildtype or predominant form of a polypeptide. An exon truncation also can result in a shift in reading frame such that an isoform is produced containing one or more amino acids not present in a wildtype or

predominant form of a polypeptide. A shift in reading frame also can result in a stop codon in the reading frame producing an isoform that terminates at a sequence different from that of a wildtype or predominant form of a polypeptide.

Alternatively spliced RNA molecules including exon modifications can produce CSR isoforms that a lack a domain or a portion thereof sufficient to reduce or remove a biological activity. For example, exon modified RNA molecules can encode shortened CSR polypeptides that lack a domain or portion thereof. Exon modified RNA molecules also can encode polypeptides where a domain is interrupted by inserted amino acids and/or by a shift in reading frame that interrupts a domain with one or more amino acids not present in a wildtype or predominant form of a polypeptide.

C. Receptor Tyrosine Kinase Isoforms

CSR isoforms provided herein include isoforms of receptor tyrosine kinases (RTKs), including receptor tyrosine kinase intron fusion proteins. The receptor tyrosine kinases (RTKs) are a large family of structurally related growth factor receptors. RTKs are involved in cellular processes including cell growth, differentiation, metabolism and cell migration. RTKs also are known to be involved in cell proliferation, differentiation and determination of cell fate. Members of the family include, but are not limited to, epidermal growth factor (EGF) receptors, platelet-derived growth factor (PDGF) receptors, fibroblast growth factor (FGF) receptors, insulin-like growth factor (IGF) receptors, nerve growth factor (NGF) receptors, vascular endothelial growth factor (VEGF) receptors, receptors to ephrin (termed Eph), hepatocyte growth factor (HGF) receptors (termed MET), TEK/Tie-2 (the receptor for angiopoietin-1), discoidin domain receptors (DDR) and others, such as Tyro3/Ax1.

Provided herein are RTK isoforms that are modified in one more domains of an RTK such that they lack a domain of an RTK or a portion of a domain sufficient to remove or reduce a biological activity of an RTK. Also provided are RTK isoforms modified at one or more amino acids of an RTK sequence such as by shortening and/or addition of one more amino acids. Additional amino acids can add a new domain or a portion thereof. RTK isoforms can be modified in a biological activity

including, but not limited to, dimerization, kinase activity, signal transduction, ligand binding, membrane association and membrane localization. RTK isoforms also can modulate a biological activity of an RTK.

1. RTK Domains and Biological Activities

RTKs have a conserved domain structure including an extracellular domain, a membrane-spanning (transmembrane) domain and an intracellular tyrosine kinase domain. The extracellular domain can bind to a ligand, such as a polypeptide growth factor or a cell membrane-associated molecule. Some RTKs have been classified as orphan receptors, having no identified ligand. Some RTKs are classified as constitutive RTKs, active without ligand binding.

Typically, dimerization of RTKs activates the catalytic tyrosine kinase domain of the receptor and subsequent activities in signal transduction. RTKs can be homodimers or heterodimers. For example, PDGF is a heterodimer composed of α and β subunits. VEGF receptors are homodimers. EGF receptors can be either heterodimers or homodimers. In another example, ErbB3, in the presence of the ligand heregulin, heterodimerizes with other members of the ErbB family (EGFR family) such as ErbB2 and ErbB3. Many RTKs are capable of autophosphorylation when dimerized, such as by transphosphorylation between subunits. Autophosphorylation in the kinase domain maintains the tyrosine kinase domain in an activated state. Autophosphorylation in other regions of the protein can influences interaction of the receptor with other cellular proteins.

RTKs interact in signal transduction pathways. For example, RTKs, when activated can phosphorylate other signaling molecules. For example, EGFR interacts in signal transduction pathways involved in processes including proliferation, dedifferentiation, apoptosis, cell migration and angiogenesis. EGFR family members can recruit signaling molecules through protein:protein interactions; some interactions involve specific binding of signaling molecules to tyrosine phosphorylated sites on the receptor. For example, the Grb2/Sos complex can bind to phosphotyrosine sites on EGFR, in turn activating the Ras/Raf/MAPK signaling cascade, which influences cell proliferation, migration and differentiation. Other exemplary signaling molecules include other RTKs, G-coupled receptors, integrins, phospholipase C,

Ca^{2+}/calmodulin-dependent kinases, transcriptional activators, cytokines and other kinases.

2. Receptor Tyrosine Kinase Isoforms

RTK isoforms lack a domain or a portion of a domain of a receptor tyrosine kinase. Thus, an RTK isoforms differs from its cognate RTK in one or more biological activities. In addition, an RTK isoform can modulate a biological activity of an RTK, such as by interacting with an RTK directly or indirectly. Biological activities include, but are not limited to, protein-protein interactions such as dimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, enzymatic activity such as kinase activity, response to regulatory molecules including regulatory proteins, cofactors, and other signaling molecules, such as in a signal transduction pathway.

RTK isoform structure and activity

In one embodiment, an RTK isoform is modified in a kinase domain. For example, an RTK isoform contains a deletion of a kinase domain or a portion thereof. The deletion need not be a deletion of the entire domain, one or more amino acids can be deleted within the domain. The deletion can be at the N-terminus of the kinase domain, the C-terminus or internally within the domain. In another example, an RTK isoform contains addition of amino acids in a kinase domain. The addition of amino acids can be at the N-terminus of the domain, the C-terminus or anywhere internally within a kinase domain.

In one aspect of the embodiment, kinase activity of an RTK isoform is altered. For example, kinase activity of an RTK isoform is reduced or eliminated. In one example, substrate specificity of the kinase activity of an RTK isoform is altered. For example, an RTK isoform is capable of autophosphorylation but not phosphorylation of other polypeptides, such as polypeptides in a signal transduction pathway. In another example, an RTK isoform phosphorylates other polypeptides but is not capable of autophosphorylation. Kinase activity of an RTK isoform can be enhanced in activity. Kinase activity of an RTK isoform can be altered in regulation. For example, the kinase activity can be constitutively active or constitutively inactive, for

example, unregulated by the addition of ligand, by receptor dimerization, by complexation such as through protein:protein interactions, and/or by autophosphorylation.

In one embodiment, an RTK isoform is modified in a transmembrane domain. For example, an RTK isoform contains a deletion of a transmembrane domain or a portion thereof. The deletion can be at the N-terminus of a transmembrane domain, the C-terminus or internally within the domain. In another example, an RTK isoform contains addition of amino acids in a transmembrane domain. The addition of amino acids can be at the N-terminus of the domain, the C-terminus or anywhere internally within the transmembrane domain.

In one aspect of the embodiments, membrane association and/or localization of an RTK isoform is altered. For example, an RTK isoform can be a soluble protein (*e.g.* not membrane localized), where a wildtype or a predominant form of the RTK is membrane localized. For example, an RTK isoform can be secreted extracellularly or localized in the cytoplasm or internally within a cellular organelle. An RTK isoform can be altered in its membrane localization. For example, an RTK isoform can associate with internal membranes, such as membranes of cellular organelles, but not the cytoplasmic membrane. An RTK isoform can be reduced in its association with a membrane, such that the proportion of membrane associated protein is altered; for example, some of the protein is soluble and some is membrane associated. An RTK isoform also can be altered in the orientation with or within a membrane compared to the orientation of a wildtype or predominant form of an RTK. For example, more or less of the polypeptide can be embedded within the membrane. More or less of the polypeptide can be associated with either side of the cellular membrane. For example, orientation can be altered such that more of the RTK isoform is found in the cytoplasm or extracellularly compared to a wildtype or predominant form of an RTK.

In one embodiment, an RTK isoform is altered in its dimerization activity. For example, an RTK-isoform homodimerizes (*i.e.* an RTK isoform: RTK isoform complex) but does not heterodimerize or is reduced in heterodimerization with a wildtype or predominant form of an RTK derived from the same gene. In another example, an RTK- isoform does not homodimerize with itself, or is reduced in

homodimerization activity but can heterodimerize with a wildtype or predominant form of an RTK from the same gene or a different gene. In another example, an RTK isoform is reduced in heterodimerization with RTKs from other genes but heterodimerizes with RTKs from the same gene.

In one embodiment, an RTK isoform is altered in its signal transduction activity. For example, an RTK isoform is altered in its association with other cellular proteins or cofactors in a signal transduction pathway. For example, an RTK isoform is altered in an interaction such as, but not limited to, an interaction with another RTK, a G-coupled receptor, an integrin, phospholipase C, a Ca^{2+}/calmodulin-dependent kinase, a transcriptional activator or regulator, a cytokine and another kinase. In another example, an RTK isoform alters signal transduction of an RTK. For example, an RTK isoform interacts with an RTK and alters its activity in signal transduction, such as by inhibiting or by stimulating signal transduction by the RTK.

In one embodiment, an RTK isoform is altered in two or more biological activities. For example, an RTK isoform is altered in kinase activity and membrane association. In another example, an RTK isoform is altered in kinase activity and dimerization. In yet another example, an RTK isoform is altered in kinase activity, dimerization and membrane association. For example, an RTK isoform is modified in a kinase domain and a transmembrane domain. In another example, insertion of addition of amino acids interrupts the kinase domain and transmembrane domains. In another embodiment, an RTK isoform is modified at a domain junction, or outside the linear sequence of amino acids for a domain and the modification alters a structure, such as the 3-dimensional structure of a domain such as a kinase domain, or a transmembrane domain.

Modulation of RTKs by RTK isoforms

RTK isoforms can modulate or alter a biological activity of an RTK, such as by interacting directly or indirectly with an RTK. Biological activities include, but are not limited to, protein-protein interactions such as dimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, enzymatic activity such as kinase activity, response to regulatory molecules including regulatory proteins, cofactors, and other

signaling molecules, such as in a signal transduction pathway. In one embodiment, interaction of an RTK isoform with an RTK, inhibits an RTK biological activity. In another embodiment, interaction of an RTK isoform with an RTK, stimulates a biological activity of an RTK.

For example, an RTK isoform competes with an RTK for ligand binding. An RTK isoform can be employed as a "ligand sponge" to remove free ligand and thereby regulate or modulate the activity of an RTK. In another example, an RTK isoform acts as a negatively acting ligand when heterodimerized or complexed with an RTK, for example, by preventing trans-autophosphorylation. An RTK isoform that lack the protein kinase domain, or a portion thereof sufficient to alter kinase activity, can inhibit activation of an RTK in a trans dominant manner.

In one embodiment, an RTK isoform acts as a competitive inhibitor of RTK dimerization. For example, an RTK isoform interacts with an RTK and prevents that RTK from homodimerizing or from heterodimerizing. An isoform that inhibits receptor dimerization can modulate downstream signal transduction pathways, such as by complexing with the receptor and inhibiting receptor activation as downstream signaling. An RTK isoform also acts as a competitive inhibitor of an RTK by competing directly with an RTK for interactions with other polypeptides and cofactors in a signal transduction pathway.

D. TNFR isoforms

CSR isoforms provided herein include isoforms of tumor necrosis factor receptors (TNFRs). TNFR isoforms lack a domain or a portion of a domain of a TNFR receptor. Thus, a TNFR isoform differs from its cognate TNFR in one or more biological activities. In addition, a TNFR isoform can modulate a biological activity of a TNFR, such as by interacting with a TNFR directly or indirectly. Biological activities include, but are not limited to, protein-protein interactions such as trimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, response to regulatory molecules including regulatory proteins, cofactors, and other signaling molecules, such as in a signal transduction pathway.

1. TNFR Domains and Biological Activities

The TNF ligand and receptor family regulate a variety of signal transduction pathways including those involved in cell differentiation, activation, and viability. TNFRs have a characteristic repeating extracellular cysteine-rich motif and a variable intracellular domain that differs between members of the TNFR family. The TNFR family of receptors includes, but is not limited to, TNFR1, TNFR2, TNFRrp, the low-affinity nerve growth factor receptor, Fas antigen, CD40, CD27, CD30, 4-1BB, OX40, DR3, DR4, DR5, and herpesvirus entry mediator (HVEM). Ligands for TNFRs include TNF- α, lymphotoxin, nerve growth factor, Fas ligand, CD40 ligand, CD27 ligand, CD30 ligand, 4-1BB ligand, OX40 ligand, APO3 ligand, TRAIL and LIGHT. TNFRs include an extracellular domain, including a ligand binding domain, a transmembrane domain and an intracellular domain that participates in signal transduction. These receptors have names. For example, TNFR1 also is referred to as p55 or p60; and TNFR2 also is referred to as p75 or p80. TNFRs are typically trimeric proteins that trimerize at the cell surface. Trimerization is important for biological activity of TNFRs.

TNFRs have a characteristic extracellular domain with a cysteine-rich motif. The extracellular domain includes a ligand binding domain. Typically, each TNFR member binds a unique ligand. A few receptors such as TNFR1 and TNFR2 and DR4 and DR5 have overlapping ligand specificity. TNFRs also trimerize. Trimerization can be induced by ligand interaction. TNFR ligands also can be trimers. Some TNFRs can be proteolytically processed to produce a secreted form of the receptor. The secreted form also trimerizes and retains certain biological activities such as ligand binding, interaction with the membrane bound form of the receptor, and inhibition of the membrane-bound form of the receptor.

TNFRs can trigger signal transduction. For example, TNFR1 activates intracellular pathways involved in apoptosis. TNFR1 trimerizes upon binding TNF ligand. Trimerization induces association of the receptor's death domains. Adapter proteins such as TRADD, TRAF-2, FADD and RIP also associate with the receptor. TRAF-2 and RIP associations activate NF-κB and JNK/AP-1pathways, including a cascade of kinases. FADD association activates a caspase cascade and subsequent apoptosis.

2. TNFR Isoform structure and activity

In one embodiment, a TNFR isoform is modified in a transmembrane domain. For example, a TNFR isoform contains a deletion of a transmembrane domain or a portion thereof. The deletion can be at the N-terminus of a transmembrane domain, the C-terminus or internally within the domain. In another example, a TNFR isoform contains addition of amino acids in a transmembrane domain. The addition of amino acids can be at the N-terminus of the domain, the C-terminus or anywhere internally within the transmembrane domain.

In one aspect of the embodiments, membrane association and/or localization of a TNFR isoform is altered. For example, a TNFR isoform can be a soluble protein (*e.g.* not membrane localized), where a wildtype or a predominant form of the TNFR is membrane localized. For example, a TNFR isoform can be secreted extracellularly or localized in the cytoplasm or internally within a cellular organelle. A TNFR isoform can be altered in its membrane localization. For example, a TNFR isoform can associate with internal membranes, such as membranes of cellular organelles, but not the cytoplasmic membrane. A TNFR isoform can be reduced in its association with a membrane, such that the proportion of membrane associated protein is altered; for example, some of the protein is soluble and some is membrane associated. A TNFR isoform also can be altered in the orientation with or within a membrane compared to the orientation of a wildtype or predominant form of a TNFR. For example, more or less of the polypeptide can be embedded within the membrane. More or less of the polypeptide can be associated with either side of the cellular membrane. For example, orientation can be altered such that more of a TNFR isoform is found in the cytoplasm or extracellularly compared to a wildtype or predominant form of a TNFR.

In one embodiment, a TNFR isoform is modified in an intracellular domain. For example, a TNFR isoform contains a deletion of an intracellular domain or a portion thereof. The deletion can be at the N-terminus of an intracellular domain, the C-terminus or internally within the domain. In another example, a TNFR isoform contains addition of amino acids in an intracellular domain. The addition of amino

acids can be at the N-terminus of the domain, the C-terminus or anywhere internally within the intracellular domain.

In one embodiment, a TNFR isoform is altered in its trimerization activity. For example, a TNFR isoform homotrimerizes (*i.e.* a TNFR isoform: TNFR isoform complex) but does not heterotrimerize or is reduced in heterotrimerization with a wildtype or predominant form of a TNFR derived from the same gene. In another example, a TNFR isoform does not homotrimerize with itself, or is reduced in homotrimerization activity but can heterotrimerize with a wildtype or predominant form of a TNFR from the same gene or a different gene. In one embodiment, a TNFR isoform acts as a competitive inhibitor of TNFR trimerization. For example, a TNFR interacts with a TNFR and prevents that TNFR from trimerizing.

In one embodiment, a TNFR isoform is altered in its signal transduction activity. For example, a TNFR isoform is altered in its association with other cellular proteins or cofactors in a signal transduction pathway. For example, a TNFR isoform is altered in an interaction such as, but not limited to, an interaction with a ligand and an adapter protein such as TRADD (TNFR-associated death domain), TRAF-2, FADD (Fas-associated death domain) and RIP (receptor interacting protein). In another example, a TNFR isoform alters signal transduction of a TNFR. For example, a TNFR isoform interacts with a TNFR and alters its activity in signal transduction, such as by inhibiting or by stimulating signal transduction by the TNFR.

In an exemplary embodiment, a TNFR isoform is altered in two or more biological activities. For example, a TNFR isoform is altered in signal transduction and membrane association. In another example, a TNFR isoform is altered in signal transduction and trimerization. In yet another example, a TNFR isoform is altered in kinase activity, trimerization and membrane association. In another embodiment, a TNFR isoform is modified in an intracellular domain and a transmembrane domain. For example, the two domains, or a portion of the domains are deleted. In another example, insertion or addition of amino acids interrupts the intracellular domain and transmembrane domains. In another embodiment, a TNFR isoform is modified at a domain junction, or outside the linear sequence of amino acids for a domain and the

modification alters a structure, such as the 3-dimensional structure of a domain such as an intracellular domain, or a transmembrane domain.

Modulation of TNFRs by TNFR isoforms

TNFR isoforms can modulate or alter a biological activity of a TNFR, such as by interacting directly or indirectly with a TNFR. Biological activities include, but are not limited to, protein-protein interactions such as trimerization, multimerization and complex formation, specificity and/or affinity for ligand, cellular localization and relocalization, membrane anchoring, response to regulatory molecules including regulatory proteins, cofactors, and other signaling molecules, such as in a signal transduction pathway. In one embodiment, interaction of a TNFR isoform with a TNFR, inhibits a TNFR biological activity. In another embodiment, interaction of a TNFR isoform with a TNFR, stimulates a biological activity of a TNFR.

For example, a TNFR isoform competes with a TNFR for ligand binding. A TNFR isoform can be employed as a "ligand sponge" to remove free ligand and thereby regulate or modulate the activity of a TNFR. In another example, a TNFR isoform acts as a negatively acting ligand when trimerized or complexed with a TNFR, for example, by preventing signal transduction and/or by inhibiting interaction with a member of a signal transduction pathway, such as adapter proteins. In one embodiment, a TNFR isoform acts as a competitive inhibitor of TNFR trimerization. For example, a TNFR isoform interacts with a TNFR and prevents that TNFR from trimerizing. An isoform that inhibits receptor trimerization can modulate downstream signal transduction pathways, such as by complexing with the receptor and inhibiting receptor activation as downstream signaling.

E. Methods for identifying and generating CSR Isoforms

CSR isoforms can be generated by analysis and identification of naturally occurring genes and expression products (RNAs) using cloning methods in combination with bioinformatics methods such as sequence alignments and domain mapping and selections.

Provided herein are methods herein for identifying and isolating CSR isoforms that utilize cloning of expressed gene sequences and alignment with a gene sequence such as a genomic DNA sequence. For example, one or more isoforms can be

isolated by selecting a candidate gene, such as a receptor tyrosine kinase. Expressed sequences, such as cDNA molecules or regions of cDNAs, are isolated. Primers can be designed to amplify a cDNA or a region of a cDNA. In one example, primers are designed which overlap or flank the start codon of the open reading frame of a candidate gene and primers are designed which overlap or flank the stop codon of the open reading frame. Primers can be used in PCR, such as in reverse transcriptase PCR (RT-PCR) with mRNA, to amplify nucleic acid molecules encoding open reading frames. Such nucleic acid molecules can be sequenced to identify those that encode an isoform. In one example, nucleic acid molecules of different sizes (*e.g.* molecular masses) from a predicted size (such as a size predicted for encoding a wildtype or predominant form) are chosen as candidate isoforms. Such nucleic acid molecules then can be analyzed, such by a method described herein, to further select isoform-encoding molecules having specified properties.

Computational analysis is performed using the obtained nucleic acid sequences to further select candidate isoforms. For example, cDNA sequences are aligned with a genomic sequence of a selected candidate gene. Such alignments can be performed manually or by using bioinformatics programs such as SIM4, a computer program for analysis of splice variants. Sequences with canonical donor-acceptor splicing sites (*e.g.* GT-AG) are selected. Molecules can be chosen which represent alternatively spliced products such as exon deletion, exon retention, exon extension and intron retention can be selected.

Sequence analysis of isolated nucleic acid molecules also can be used to further select isoforms that retain or lack a domain and/or biological function compared to a wildtype or predominant form. For example, isoforms encoded by isolated nucleic acid molecules can be analyzed using bioinformatics programs such as described herein to identify protein domains. Isoforms then can be selected which retain or lack a domain or a portion thereof.

In one embodiment of the method, isoforms are selected that lack a transmembrane domain or portion thereof sufficient to lack or significantly reduce membrane localization. For example, isoforms are selected that are shortened before a transmembrane domain or that are shortened within a transmembrane domain.

Isoforms also can be selected that lack a transmembrane domain or portion thereof and have one or more amino acids operatively linked in place of the missing domain or portion of a domain. Such isoforms can be the result of alternative splicing events such as exon extension, intron retention, exon deletion and exon insertion. In some case, such alternatively spliced RNA molecules alter the reading frame of an RNA and/or operatively link sequences not found in an RNA encoding a wildtype or predominant form. Isoforms also can be selected that lack a kinase domain or portion thereof. Isoforms can be selected that lack a kinase domain or portion thereof and also lack a transmembrane domain or portion thereof. Isoforms also can be selected that lack a multimerization domain, such as a dimerization or trimerization domain, and/or an intracellular domain that interacts with and participates in signal transduction activity.

For example, nucleic acid molecules encoding candidate RTK isoforms can be further selected for isoforms that lack a kinase domain, a transmembrane domain, an extracellular domain or a portion thereof. Nucleic acid molecules can be selected which encode an RTK isoform and have a biological activity that differs from a wildtype or predominant form of an RTK. In one example, RTK isoforms are selected that lack a transmembrane domain such that the isoforms are not membrane localized and are secreted from a cell. In another example, TNFR isoforms are identified and selected that lack a transmembrane domain, or a portion thereof. TNFR isoforms also can be selected that lack an intracellular domain or that lack an intracellular domain and a transmembrane domain.

Allelic Variants of Isoforms

Allelic variants of CSR isoform sequences can be generated or identified that differ in one or more amino acids from a particular CSR isoform. Allelic variation occurs among members of a population or species and also between species. For example, isoforms can be derived from different alleles of a gene; each allele can have one or more amino acid differences from the other. Such alleles can have conservative and/or non-conservative amino acid differences. Allelic variants also include isoforms produced or identified from different subjects, such as individual subjects or animal models or other animals. Amino acid changes can result in

modulation of an isoform biological activity. In some cases, an amino acid difference can be "silent," having no or virtually no detectable effect on a biological activity. Allelic variants of isoforms also can be generated by mutagenesis. Such mutagenesis can be random or directed. For example, allelic variant isoforms can be generated that alter amino acid sequences or a potential glycosylation site to effect a change in glycosylation of an isoform, including alternate glycosylation, increased or inhibition of glycosylation at a site in an isoform. Allelic variant isoforms can be at least 90% identical in sequence to an isoform. Generally, an allelic variant isoform from the same species is at least 95%, 96%, 97%, 98%, 99% identical to an isoform, typically an allelic variant is 98%, 99%, 99.5% identical to an isoform.

F. Exemplary CSR Isoforms

The methods herein can be used to generate CSR isoforms from a variety of genes. One exemplary group of genes is receptor tyrosine kinases. Receptor tyrosine kinases (RTKs) are a large collection of genes and encoded polypeptides that can be grouped into families based on, for example, structural arrangements of sequence motifs in the polypeptides. For example, structural motifs in the extracellular domains such as, immunoglobulin, fibronectin, cadherin, epidermal growth factor and kringle repeats can be used to group RTKs. Such classification by structural motifs has identified greater then 16 families of RTKs, each with a conserved tyrosine kinase domain. Examples of RTKs include, but are not limited to, erythropoietin-producing hepatocellular (EPH) receptors (also referred to as ephrin receptors), epidermal growth factor (EGF) receptors, fibroblast growth factor (FGF) receptors, platelet-derived growth factor (PDGF) receptors, vascular endothelial growth factor (VEGF) receptors, cell adhesion RTKs (CAKs), Tie/Tek receptors, hepatocyte growth factor (HGF) receptors (termed MET), TEK/Tie-2 (the receptor for angiopoietin-1), discoidin domain receptors (DDR), insulin growth factor (IGF) receptors, insulin receptor-related (IRR) receptors and others, such as Tyro3/Ax1. Exemplary genes encoding RTKs include, but are not limited to, ErbB2, ErbB3, DDR1, DDR2, EGFR, EphA1, EphA2, EphA3, EphA 4, EphA 5, EphA 6, EphA 7, EphA8, EphB1, EphB2, EphB3, EphB4, EphB5, EphB6, FGFR-1, FGFR-2, FGFR-3, FGFR-4, Flt1 (also known as VEGFR-1), VEGFR-2, VEGFR-3 (also known as

VEGFRC), MET, RON, PDGFR-A, PDGFR-B, CSF1R, Flt3, KIT, TIE-1 and TEK (also known as TIE-2) and genes encoding the RTKs noted above and not set forth.

RTKs participate in a variety of signal transduction pathways. RTKs regulate critical cellular processes including cell proliferation, dedifferentiation, apoptosis, cell migration and angiogenesis. RTK activation and thus subsequent activation of a signal transduction pathway is generally dependent on receptor activation, such as by activation of the receptor by ligand binding and autophosphorylation. RTKs can be subject to misregulation leading to misregulation of signal transduction. Such misregulation is associated with a number of diseases and conditions. Alternatively, certain RTKs are expressed on cells and lead to or participate in alteration in cellular activities, such as oncogenic transformation. Such expression and/or misregulation is associated with a number of diseases and conditions, including but not limited to diseases involving abnormal cell proliferation, such as neoplastic diseases, restenosis, disease of the anterior eye, cardiovascular diseases, obesity and a variety of others.

RTK isoforms provided herein and generated by methods provided herein can be used to modulate a biological activity of an RTK, such as an RTK endogenous to a particular cell type or tissue. The ability to modulate a biological activity of an RTK allows re-regulation of misregulated RTKs as well as directed regulation of cellular pathways in which RTKs participate. Modulating a biological activity of an RTK includes direct modulation, whereby an RTK isoform interacts with an RTK, such as by complexation with an RTK, modulation of homodimerization and/or heterodimerization of an RTK and/or modulation of trans-phosphorylation of an RTK, including inhibition of phosphorylation of an RTK. Modulation of an RTK also includes indirect modulation whereby an RTK isoform indirectly affects a biological activity of an RTK. Indirect modulation includes isoforms that act as a "ligand sponge," competing for ligand binding with an RTK. Indirect modulation also includes interactions of an isoform with signaling molecules in a signaling pathway, thus modulating the activity such as by competition with interactions of such signaling molecules with an RTK. Exemplary RTK isoforms and uses of such RTK isoforms in targeting and regulating RTK activity are described below.

1. EGFR

EGFR (epidermal growth factor receptor) is a 170 kDa protein that binds to EGF, a small, 53 amino acid protein-ligand that stimulates the proliferation of epidermal cells and a variety of other cell types. EGF receptors are widely expressed in epithelial, mesenchymal and neuronal tissues and play important roles in proliferation and differentiation. EGF Receptor is characterized by several functional domains. The EGFR protein (GenBank No. NP_005219 set forth as SEQ ID NO:252 is characterized by two Receptor L Domains between amino acids 57 – 168 and amino acids 361 – 481. Receptor L Domains make up the bilobal ligand binding site. A Furin-like cysteine rich region, typically involved in the signal transduction mechanism of receptor tyrosine kinases and receptor aggregation, can be found in EGFR between amino acids 184 – 338. The transmembrane domain of EGFR lies between amino acids 646 – 668 and protein kinase domain lies between amino acids 712 – 968.

EGFR polypeptides include allelic variants of EGFR. For example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:252. For example, one or more amino acid variations can occur in the protein kinase domain of EGFR. An allelic variant can include amino acid changes at position 719 where, for example, G is replaced by C, or at position 858 where, for example, L is replaced by R, or at position 861 where, for example, L is replaced by Q. An allelic variation also can include one or more amino acid changes, such as at position 521 (SNP NO: 11543848) where, for example, R can be replaced by K. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:252 and the variant exhibits a change in biological activity. Amino acid changes occurring in the protein kinase domain, such as at position 719, 858, or 861, can be associated with a response to Gefitinib in patients with non-small-cell lung cancer indicating an essential role of the EGFR signaling pathway in the tumor, or, such as at position 858, can be associated with enhanced activity of the EGFR receptor in response to EGF as assessed by autophosphorylation of EGFR. An exemplary EGFR allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 288.

EGF receptors are encoded by a family of related genes known as also erbB genes (*e.g.* ErbB2, ErbB3, ErbB4) and HER genes (*e.g.* Her-2). The EGF receptor family includes four members, EGF-receptor (HER-1; ErbB1), human epidermal growth factor receptor-2 (HER-2; ErbB2), HER-3 (ErbB3) and HER-4 (ErbB4). The ligand for EGFR/HER-1 is EGF, while the ligand for HER-2, HER-3 and HER-4 is neuregulin-1 (NRG-1). NRG-1 preferentially binds to either HER-3 or HER-4 after which the bound receptor subunit heterodimerizes with HER-2. HER-4 also is capable of homodimerization to form an active receptor.

Misregulation of the ErbB family has been implicated in a number of different types of cancer. For example, overexpression of EGFR is associated with a number of human tumors including, but not limited to, esophageal, stomach, bladder and colon cancers, gliomas and meningiomas, squamous carcinoma of the lungs, and ovarian, cervical and renal carcinomas. Using the methods provided herein, RTK isoforms and pharmaceutical compositions containing RTK isoforms can be generated for use as therapeutic agents which target and re-regulate misregulation of EGF receptors.

a. ErbB2

ErbB2 is a member of the EGF receptor family. The ErbB2 protein (GenBank No. NP_004439 set forth as SEQ ID NO:266) is characterized by two Receptor L Domains between amino acids 52 – 173 and amino acids 366 – 486; a Furin-like cysteine rich region between amino acids 189 – 343; the transmembrane domain between amino acids 653 – 675; and protein kinase domain between amino acids 720 – 976. A ligand that binds with high affinity has not been identified for ErbB2. Instead, ErbB3 or ErbB4 when bound by ligand (NRG-1) heterodimerize with ErbB2 to form an active receptor dimer. In addition, ErbB2 exhibits constitutive activity (homodimerization and kinase activity) in the absence of ligand. In addition, overexpression of ErbB2 is capable of cell transformation. ErbB2 overexpression has been identified in a variety of cancers, including breast, ovarian, gastric and endometrial carcinomas. Thus, targeting ErbB2 homodimers can regulate ErbB2 homodimerization. For example, an ErbB2 RTK isoform can target and

down-regulate ErbB2 overexpression. Additionally, an ErbB2 RTK- isoform can target ErbB3 and/or ErbB4 through heterodimerization.

ErbB2 proteins include allelic variants of ErbB2. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:266. For example, one or more amino acid variations can occur in the transmembrane domain of ErbB2. An allelic variant can include amino acid changes at position 655 where, for example, I is replaced by V. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:266 and the variant exhibits a change in a biological activity. Amino acid changes occurring in the transmembrane domain of ErbB2, such as at position 655, can be associated with increased risk of prostate cancer, gastric cancer, or breast cancer. An exemplary ErbB2 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 299.

Provided herein are exemplary ErbB2 isoforms that lack one or more domains or a part thereof compared to a cognate ErbB2 such as set forth in SEQ ID NO:266. Included are exemplary ErbB2 isoforms that lack a transmembrane domain and lack a kinase domain, such as the polypeptides set forth in SEQ ID NOS: 96-98 and 108. Such isoforms can contain other domains of ErbB2. For example, the exemplary ErbB2 isoform set forth as SEQ ID NO: 96 is characterized by two Receptor L Domains between amino acids 54 – 175 and amino acids 368 – 488, and a Furin-like cysteine rich region between amino acids 191 – 345. The exemplary ErbB2 isoform set forth as SEQ ID NOS: 97 and 98 are characterized by two Receptor L Domains between amino acids 52 – 173 and amino acids 366 – 486, and a furin-like cysteine rich region between amino acids 189 – 343. The exemplary ErbB2 isoform set forth as SEQ ID NO: 108 is characterized by a portion of a Receptor L Domain between amino acids 52 – 75.

ErbB2 isoforms can be used to modulate RTKs such as in the treatment of cancers characterized by the overexpression of EGFR receptors such as those characterized by overexpression of ErbB2 and/or ErbB3. ErbB2 isoforms can be used as a treatment for autoimmune diseases which involve EGFR family members in the maintenance of inflammation and hyperproliferation, including asthma. ErbB2

isoforms also can be used to target RTKs in conditions including Menetrier's disease, Alzheimer's disease and as modulators, for example as an antagonist for bone resorption.

b. ErbB3

ErbB3 also is a member of the EGF receptor family involved in regulating development of neuronal survival and synaptogenesis, astrocytic differentiation and microglial activation. The ErbB3 protein (GenBank No. NP_001973 set forth as SEQ ID NO:267) is characterized by two Receptor L Domains between amino acids 55 – 167 and between amino acids 353 – 474; a Furin-like cysteine rich region between amino acids 180 – 332; transmembrane domain between amino acids 644 – 666; and protein kinase domain between amino acids 709 – 965. The ligand for ErbB3 is NRG-1. Although NRG-1 can bind to ErbB3 and ErbB4, ErbB3 binds NRG-1 with an affinity an order of magnitude lower than ErbB4. ErbB3 has lower tyrosine kinase activity compared to other members of the EGFR family. It is capable of recruiting alternative signaling molecules, for example, phosphatidylinositol-3 kinase. ErbB3 overexpression has been implicated in a number of human cancers such as breast, lung and bladder cancers and adenocarcinomas.

ErbB3 isoforms can be used to target RTKs such as in the treatment of cancers characterized by the overexpression of EGFR receptors such as those characterized by overexpression of ErbB2 and/or ErbB3. ErbB3 isoforms can target ErbB3 homodimers. ErbB3 isoforms can target ErbB2 through heterodimerization of an ErbB3 isoform with ErbB2. ErbB3 isoforms can be used for treatment of diseases and conditions in which EGFR receptors are involved. For example, ErbB3 isoforms can be used as a treatment for autoimmune diseases which involve EGFR family members in the maintenance of inflammation and hyperproliferation, including asthma. ErbB3 isoforms also can be used to target RTKs in conditions including Menetrier's disease, Alzheimer's disease and as modulators, for example as an antagonist for bone resorption.

2. Discoidin Domain Receptors - DDR1

Discoidin domain receptors (*e.g.* DDR-1) are a family of RTKs that are thought to play a role in cell adhesion. The DDR1 protein (GenBank No. NP_054699

set forth as SEQ ID NO: 250) is characterized by a F5/8 type C domain, also known as the discoidin (DS) domain, between amino acids 46 – 182; the transmembrane domain between amino acids 417 – 439; and protein kinase domain between amino acids 610 – 913. The discoidin domain is a unique structural motif in the extracellular domain that is homologous to the *Dictyostelium discoideum* (slime mold) protein discoidin-1, a carbohydrate-binding protein involved in cell aggregation. The discoidin-like domain, although not found in other RTKs, is found in other extracellular molecules that are known to interact with cellular membrane proteins (*e.g.*, coagulation factors V and VIII).

DDR1 proteins include allelic variants of DDR1. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:250. For example, one or more amino acid variations can occur in the F5/8 type C or discoidin domain of DDR1. An allelic variant can include amino acid changes at position 53 where, for example, W can be replaced by A, or at position 55 where, for example, D can be replaced by A, or at position 66 where, for example, S can be replaced by A, or at position 68 where, for example, D can be replaced by A, or at position 105 where, for example, R can be replaced by A, or at position 106 where, for example, H can be replaced by A, or at position 110 where, for example, L can be replaced by A, or at position 112 where, for example, K can be replaced by A, or at position 173 where, for example, V can be replaced by A, or at position 174 where, for example, M can be replaced by A, or at position 175 where, for example, S can be replaced by A. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:250 and the variant exhibits a change in a biological activity. Amino acid changes occurring in the discoidin domain of DDR1, such as those at position 105 and 175, can result in reduced activation and phosphorylation of DDR1 due to an inability to bind to collagen. Other amino acid changes in the discoidin domain of DDR1, such as those at positions 106, 173, and 174, can result in a marked reduction in the ability of DDR1 to bind to collagen. An exemplary DDR1 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 286.

DDRs are widely expressed in fetal and adult organs and tissues. DDR1 is expressed primarily in epithelial cells in brain, lung, kidney and gastrointestinal tract, whereas DDR2 is expressed in brain, heart, and muscle. DDR also may play an important role in brain development. DDR tyrosine kinases have been linked to human cancers. For example, DDR1 can bind to collagen (*e.g.* types I through VI) and mediate collagen-induced activation of matrix metalloproteinase-1. Matrix metalloproteinase-1 is involved in the degradation of extracellular matrix, which allows neoplastic cells to metastasize. Overexpression of DDR-1 has been linked to cancers such as breast, ovarian and esophageal cancers and a variety of central nervous system neoplasms, such as pediatric brain cancers. Activation of DDR1 also has been implicated in inflammatory responses.

Exemplary DDR isoforms include DDR1 isoforms set forth in SEQ ID NO: 106, 115 and 117. These exemplary DDR1 isoforms lack one or more domains or a part thereof compared to a cognate DDR1 such as set forth in SEQ ID NO:250. The exemplary DDR1 isoforms set forth as SEQ ID NOS: 106, 115, and 117 contain an F5/8 type C domain between amino acids 46 – 182, and lack the transmembrane and protein kinase domains.

DDR1 isoforms, including DDR1 isoforms herein, can include allelic variation in the DDR1 polypeptide. For example, a DDR1 isoform can include one or more amino acid differences present in an allelic variant. In one example, a DDR1 isoform includes one or more allelic variation as set forth in SEQ ID NO:286. Examples of allelic variation include variants in the F5/8 type C and discoidin domains, including, but not limited to amino acid variation at positions corresponding to amino acids 53, 55, 66, 68, 105, 106, 110, 113, 173, 174, or 175 of SEQ ID NO:286.

DDR-1 isoforms can be used to modulate DDR-1 RTK. For example, a DDR-1 isoform can be used to down regulate DDR-1 overexpression and or activation in diseases and conditions in which DDR-1 is involved.

3. Eph Receptors

Eph receptors (erythropoietin-producing hepatocellular receptors; also referred to as ephrin receptors) are the largest known family of RTKs. The ligands for Eph receptors are ephrins (Eph receptor interacting protein). The Eph and Ephrin system

includes at least fourteen Eph receptor tyrosine kinase proteins and nine ephrin membrane ligands. The Eph receptors and Ephrin membrane proteins play important roles in disease and development (see, *e.g.*, Figure 1). For example, binding of cell surface Eph and ephrin proteins results in bi-directional signals that regulate the cytoskeletal, adhesive and motile properties of the interacting cells. Through these signals Eph and Ephrin proteins are involved in early embryonic cell movements, which establish the germ layers, and in cell movements involved in formation of tissue boundaries and the pathfinding of axons. Ligand and receptor are membrane-bound molecules and signaling can occur through either protein. The ephrins have been separated into two classes based on the manner in which they are anchored to the cell membrane; type A ligands are linked to the cell membrane by a glycosylpho-phatidylinositol (GPI) linkage and type B ligands encode for a transmembrane domain. Eph receptors include, but are not limited to, EphA1, EphA2, EphA3, EphA4, EphA5, EphA6, EphA7, EphA8, EphB1, EphB2, EphB3, EphB4, EphB5, EphB6.

Ephrin receptors are characterized by a cytoplasmic tyrosine kinase domain, a conserved cysteine-rich domain, two fibronectin type III domains and an immunoglobulin-like N-terminal ligand binding domain. Further, two tyrosine residues near the transmembrane domain are highly conserved and phosphorylated in response to ligand binding and appear to be critical for enzymatic function. Other sites of protein-protein interaction also are mediated by sterile alpha motifs and postsynaptic density protein, disc large, zona occludens binding motifs located near the C-terminal end of some Eph receptors. Sterile alpha motifs (SAM) mediate cell-cell initiated signal transduction via the binding of SH2-containing proteins to a conserved tyrosine that is phosphorylated and in many cases mediates homodimerization.

The Eph family of RTKs is involved in a variety of cellular processes, including embryonic patterning, neuronal targeting, vascular development and angiogenesis. Particularly due to a role in angiogenesis, Eph receptors have been implicated in human cancers, such as breast cancer. Misregulation of EphA receptors also are involved in pathological conditions. For example, upregulation of the EphA

receptor tyrosine kinase stimulates vascular endothelial cell growth factor (VEGF) - induced angiogenesis, common in certain eye diseases, rheumatoid arthritis and cancer. An EphA isoform, such as an isoform acting as an EphA receptor antagonist can be used to block or inhibit inappropriate angiogenesis. EphB receptors have been implicated in cancers such as colorectal cancers. EphB receptors also play a role in dendritic spine development (post-synaptic targets for excitatory synapses) and may be implicated in neurodegenerative disorders. Exemplary EphA and EphB isoforms are set forth in SEQ ID NOS: 107, 149, 151, 153, 155, 168, 170, 172, and 174.

a. EphA1

EphA1 is a type A Eph receptor. The EphA1 protein (GenBank No. NP_005223 set forth as SEQ ID NO:253) is characterized by an Ephrin ligand binding domain between amino acids 27 – 204, two fibronectin type III domains between amino acids 333 – 431 and between amino acids 448 – 528; a transmembrane domain between amino acids 548 – 570; protein kinase domain between amino acids 624 – 880, and two SAM domains (SAM-1 between amino acids 911 – 975, and SAM-2 between amino acids 910 – 976) at the carboxy terminus.

EphA1 proteins include allelic variants of EphA1. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:253, such as the allelic variations set forth in SEQ ID NO:289. One or more amino acid variations can occur, for example, in the ephrin ligand binding domain of EphA1, such as an amino acid change at position 160 where, for example, A can be replaced by V.

Type A Eph receptors bind to type A ephrins, which are linked to cell membranes via a GPI anchor. EphA1 is expressed widely in differentiated epithelial cells, including skin, adult thymus, kidney and adrenal cortex. Overexpression of EphA1 has been implicated in a variety of human cancers, including head and neck cancer. EphA1 isoforms can be used to target such diseases and other conditions in which Eph receptors have been implicated.

Exemplary EphA1 isoforms include EphA1 isoforms set forth in SEQ ID NOS: 107, 149, 151, and 153. These exemplary EphA1isoforms lack one or more domains or a part thereof compared to a cognate EphA1 such as set forth in SEQ ID

NO:253. The exemplary EphA1 isoforms set forth as SEQ ID NOS:149 and 153 contain an ephrin ligand binding domain between amino acids 27 – 204 and one of two fibronectin type III domains between amino acids 333 – 431. The isoform set forth as SEQ ID NO: 149 lacks a fibronectin type III domain, a transmembrane domain, protein kinase domain, and two SAM domains compared to the cognate receptor. The exemplary EphA1 isoform set forth as SEQ ID NO: 151 contains the ephrin ligand binding domain between amino acids 27 – 204, but does not contain fibronectin type III domains, transmembrane domain, protein kinase domain and SAM domains. The exemplary EphA1 isoform set forth as SEQ ID NO: 107 contains the ephrin ligand binding domain between amino acids 1 – 114, but does not contain fibronectin type III domains, transmembrane domain, protein kinase domain and SAM domains.

EphA1 isoforms, including EphA1 isoforms herein, can include allelic variation in the EphA1 polypeptide. For example, an EphA1 isoform can include one or more amino acid differences present in an allelic variant. In one example, an EphA1 isoform includes one or more allelic variations as set forth in SEQ ID NO:289. An allelic variation can include one or more amino acid changes in the ephrin ligand binding domain, such as at position 160.

b. EphA2

EphA2 binds ephrin-A3, ephrin-A1, ephrin-A4, an ephrin-A2. EphA2 expression is frequently elevated in cancer and is highly expressed in tumor tissues including breast, prostate, non-small cell lung cancers, colon, kidney, lung, ovary, stomach, uterus, and aggressive melanomas. EphA2 has also been found in Schwann cells, the primitive streak and hindbrain in restricted expression pattern. It has been suggested that EphA2 does not simply function as a marker, but as an active participant in malignant progression. The normal cellular functions of EphA2 are not well understood, but tumor-based models suggests potential roles for EphA2 in the regulation of cell growth, survival, migration, and angiogenesis.

The EphA2 receptor set forth as SEQ ID NO:254 (GenBank No. NP_004422) is characterized by an ephrin ligand binding domain between amino acids 28 – 201, two fibronectin type III domains between amino acids 329 – 424 and between amino

acids 436 – 519, a transmembrane domain between amino acids 536 – 558, protein kinase domain between amino acids 613 – 871; and two SAM domains (SAM-1 between amino acids 902 – 966, and SAM-2 between amino acids 901 – 968) at the carboxy terminus.

EphA2 proteins include allelic variants of EphA2. In one example, an allelic variant contains one or more amino acid changes compared to positions corresponding to the amino acid sequence set forth as SEQ ID NO:254. For example, one or more amino acid variations can occur in the ephrin ligand binding domain of EphA2. An allelic variant can include amino acid changes at position 94 (SNP NO: 1058370) where, for example, I can be replaced by N, or at position 96 (SNP NO: 1058371) where, for example, I can be replaced by F, or at position 99 (SNP NO: 1058372) where, for example, K can be replaced by N. Additional examples of allelic variation can occur in the fibronectin type III domain. An allelic variant can include amino acid changes at position 350 (SNP NO: 11543934) where, for example, P is replaced by T. One or more amino acid variations also can occur in the protein kinase domain. An allelic variant can include amino acid changes at position 825 where, for example, E can be replaced by K. An exemplary EphA2 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 290.

Exemplary EphA2 isoforms lack one or more domains or a part thereof compared to a cognate EphA2 such as set forth in SEQ ID NO:254. The exemplary EphA2 isoform set forth as SEQ ID NO: 168 contains an ephrin ligand binding domain between amino acids 28 – 201, a fibronectin type III domain between amino acids 329 – 424 and a portion of another fibronectin type III domain between amino acids 436 – 497. SEQ ID NO: 168 does not contain the transmembrane, protein kinase, and SAM domains. EphA2 isoforms, including EphA2 isoforms herein, can include allelic variation in the EphA2 polypeptide. For example, an EphA2 isoform can include one or more amino acid difference present in an allelic variant. In one example, an EphA2 isoform includes one or more allelic variations as set forth in SEQ ID NO:290. An allelic variation can include a position corresponding to amino acid positions 94, 96, or 99 in SEQ ID NO:254, or for example, in the fibronectin type

III domain, such as at a position corresponding to amino acid 350 in SEQ ID NO:254.

c. EphA8

EphA8 is a type A Eph receptor. Type A Eph receptors bind to type A ephrins, which are linked to cell membranes via a GPI anchor. EphA8 has been implicated in cell migration and cell adhesion as well as nervous system development, including axon guidance. EphA8 isoforms can be used to target such diseases and other conditions in which Eph receptors have been implicated.

The EphA8 receptor (GenBank No. NP_065387 set forth as SEQ ID NO:260) is characterized by an Ephrin ligand binding domain between amino acids 31 – 204, two fibronectin type III domains between amino acids 329 – 425 and amino acids 437 – 524, a transmembrane domain between amino acids 541 – 563, protein kinase domain between 635 – 892 and two SAM domains (SAM-1 between amino acids 931 – 992 and SAM-2 between amino acids 927 – 994).

EphA8 proteins include allelic variants of EphA8. In one example, an allelic variant contains one or more amino acid changes compared to positions corresponding to the amino acid sequence set forth as SEQ ID NO:260. For example, one or more amino acid variations can occur in the fibronectin type III domain of EphA8. An allelic variant can include amino acid changes at position 444 (SNP NO: 2295021) where, for example, V can be replaced by M. Allelic variations also can occur at position 301 (SNP NO: 638524) where, for example, A can be replaced by V, or at position 612 (SNP NO:999765) where, for example, E can be replaced by Q. An exemplary EphA8 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 293.

d. EphB1

EphB1 has been shown to bind to ephrin-B2, ephrin-B1, ephrin-A3, ephrin-A1 and ephrin-B3. EphB1 is expressed in developing and adult neural tissue. EphB1 signaling pathways impact responses relevant to vascular development, including cell attachment, migration and capillary-like assembly responses.

The EphB1 protein (GenBank No. NP_004432 set forth as SEQ ID NO:261) is characterized by an Ephrin ligand binding domain between amino acids 19 – 196,

two fibronectin type III domains between amino acids 323 – 414 and between amino acids 434 – 518, transmembrane domain between amino acids 541 – 563, protein kinase domain between amino acids 619 – 878, and two SAM domains (SAM-1 between amino acids 909 – 973, and SAM-2 between amino acids 908 – 975) at the carboxy terminus.

EphB1 proteins include allelic variants of EphB1. In one example, an allelic variant contains one or more amino acid changes compared to positions corresponding to the amino acid sequence set forth as SEQ ID NO:261. For example, one or more amino acid variations can occur in the ephrin ligand binding domain of EphB1. An allelic variant can include amino acid changes at position 87 (SNP NO:1042794) where, for example, T can be replaced by S, or at position 152 (SNP NO:1042793 where, for example, G can be replaced by R. Additional examples of amino acid changes can occur in the fibronectin type III domain. An allelic variant can include amino acid changes at position 367 (SNP NO:1042789) where, for example, R is replaced by G, or at position 485 (SNP NO:1042788) where, for example, R is replaced by S. One or more amino acid changes also can occur in the protein kinase domain. An allelic variant can include amino acid changes at position 813 (SNP NO:1042786) where, for example, V can be replaced by I, or at position 847 (SNP NO:1042785) where, for example, M can be replaced by T. Another example of amino acid changes can occur in the SAM domain. An allelic variant can include amino acid changes at position 973 (SNP NO:1042784) where, for example, R is replaced by W. Allelic variations also can occur at position 274 (SNP NO:1126906) where, for example, T is replaced by R. An exemplary EphB1 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 294.

Exemplary EphB1isoforms lack one or more domains or a part thereof compared to a cognate EphB1 such as set forth in SEQ ID NO:261. The exemplary EphB1 isoform set forth as SEQ ID NO: 155 contains a portion of an ephrin ligand binding domain between amino acids 19 – 167 and lacks fibronectin type III domains, transmembrane domain, protein kinase domain, and SAM domains compared with a cognate EphB1 receptor (*e.g.* SEQ ID NO:261).

EphB1 isoforms, including EphB1 isoforms herein, can include allelic variation in the EphB1 polypeptide. For example an EphB1 isoform can include one or more amino acid differences present in an allelic variant. In one example, an EphB1 isoform includes one or more allelic variation as set forth in SEQ ID NO:294. An allelic variation can include one or more amino acid changes in the ephrin ligand binding domain, such as positions corresponding to amino acid positions 87 and 152 of SEQ ID NO:261.

e. EphB4

EphB4 receptors bind to ephrin-B2 and ephrin-B1 proteins. Ephrin-B proteins transduce signals, such that bidirectional signaling can occur upon interaction with Eph receptor.

The EphB4 receptor polypeptide (GenBank No. NP_004435 set forth as SEQ ID NO:264) is characterized by an ephrin ligand binding domain between amino acids 17 – 197, two fibronectin type III domains between amino acids 324 – 414 and between amino acids 434 – 519, transmembrane domain between amino acids 541 – 563, cytoplasmic protein kinase domain between 615 – 874, and two SAM domains (SAM-1 between amino acids 905 – 969, and SAM-2 between amino acids 904 – 971) at the carboxy terminus.

EphB4 proteins can include allelic variants of EphB4. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:264. For example, one or more amino acid variations can occur in the fibronectin type III domain of EphB4. An allelic variant can include amino acid changes at position 463 (SNP NO:7457245) where, for example, A can be replaced by D, or at position 471 (SNP NO:3891495) where, for example, Y can be replaced by D. Additional amino acid changes can occur in the SAM domain. An allelic variant can include amino acid changes at position 926 (SNP NO:1056997) where, for example, E can be replaced by D. An exemplary EphB4 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 297.

Exemplary EphB4 isoforms include the EphB4 isoforms set forth in SEQ ID NO: 170, 172 and 174. These exemplary EphB4 isoforms lack one or more domains or a part thereof compared to a cognate EphB4 such as set forth in SEQ ID NO:264.

The exemplary EphB4 isoform set forth as SEQ ID NO: 170 contains an ephrin ligand binding domain between amino acids 17 – 197. SEQ ID NO: 170 does not contain fibronectin type III domains, transmembrane domain, protein kinase domain, and SAM domains. The exemplary EphB4 isoform set forth as SEQ ID NO: 172 contains an ephrin ligand binding domain between amino acids 17 – 197, a fibronectin type III domain between amino acids 324 – 414 and a portion of another fibronectin type III domain between amino acids 434 – 514. SEQ ID NO: 172 does not contain the transmembrane domain, protein kinase domain, and SAM domains. The exemplary EphB4 isoform set forth as SEQ ID NO: 174 contains an ephrin ligand binding domain between amino acids 17 – 197 and a portion of a fibronectin type III domain between amino acids 324 – 413. SEQ ID NO: 174 does not contain the second fibronectin type III domain, transmembrane domain, protein kinase domain, and SAM domains.

EphB4 isoforms, including EphB4 isoforms herein, can include allelic variation in the EphB4 polypeptide. For example an EphB4 isoform can include one or more amino acid differences present in an allelic variant. In one example, an EphB4 isoform includes one or more allelic variation as set forth in SEQ ID NO:297. An allelic variation can include one or more amino acid changes in the fibronectin type III domain, such as at positions corresponding to amino acid positions 463 or 471 of SEQ ID NO:264.

4. Fibroblast Growth Factor Receptors

The fibroblast growth factor receptor (FGFR) family includes FGFR-1, FGFR-2, FGFR-3, FGFR-4 and FGFR-5. There are at least 23 known FGF proteins that are capable of binding to one or more FGF receptors. FGF receptors are structurally characterized by three N-terminal Ig-like domains (extracellular), a transmembrane domain and the split tyrosine-kinase domain at the C-terminus (cytoplasmic). FGFs and their receptors are involved in stimulation of cellular proliferation, promoting angiogenesis and wound healing, and modulating cell motility and differentiation. FGFRs have been implicated in a variety of human cancers as well as diseases of the eye.

a. FGFR-1

FGFR-1 has specificity for FGF-1, -2, and -4 and is expressed in a number of cell types including fibroblasts, endothelial cells, certain epithelial cells, vascular smooth muscle cells, lymphocytes, macrophages, and numerous tumor cells.

The FGFR-1 polypeptide (GenBank No. AAA35835 set forth as SEQ ID NO:268) is characterized by three immunoglobulin-like domains; domain 1 between amino acids 35 – 119, domain 2 between amino acids 156 – 246, and domain 3 between amino acids 253 – 357. FGFR-1 also has a transmembrane domain between amino acids 375 – 397 and protein kinase domain between amino acids 476 – 752.

FGFR-1 proteins include allelic variants of FGFR-1. In one example, an allelic variant contains one or more amino acid changes compared to positions corresponding to the amino acid sequence set forth as SEQ ID NO:268. For example, one or more amino acid variations can occur in the immunoglobulin domain of FGFR-1. An allelic variant can include amino acid changes at position 97 where, for example, G can be replaced by D, or at position 99 where, for example, Y can be replaced by C, or at position 165 where, for example, A can be replaced by S, or at position 190 where, for example, K can be replaced by E, or at position 192 where, for example, S can be replaced by G, or at position 198 where, for example, D can be replaced by G, or at position 275 where, for example, C can be replaced by Y. Additional amino acid changes can occur in the protein kinase domain. An allelic variant can include amino acid changes at position 605 where, for example, V can be replaced by M, or at position 664 where, for example, W can be replaced by R, or at position 717 where, for example, M can be replaced by R. One or more amino acid change also can occur at position 22 where, for example, R can be replaced by S, or at position 250 where, for example P can be replaced by R, or at position 770 where, for example, P can be replaced by S, or at position 816 where, for example G can be replaced by R, or at position 820 where, for example, R can be replaced by C. In one example, an allelic variant includes one or more amino acid change compared to SEQ ID NO:268 and the variant exhibits a change in a biological activity. Polypeptides containing amino acid changes in either the immunoglobulin or protein kinase domain of FGFR-1, such as those at positions 97, 99, 165, 275, 605, 664, or 717, can be characterized as loss-of function mutations. In the context of a cognate receptor (such

as SEQ ID NO: 268) such changes cause autosomal dominant Kallmann syndrome. Amino acid changes occurring in the protein kinase domain, such as at position 717, can impair PLC gamma association with the receptor and inhibit FGF-mediated phosphotidylinositol and Ca2+ mobilization; these changes, however, do not affect FGF-mediated mitogenesis. Additional allelic variants, such at position 250, can be associated with autosomal dominant skeletal disorders such as Pfeiffer syndrome. An exemplary FGFR-1 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO:300.

Exemplary FGFR-1 isoforms include FGFR-1 isoforms set forth in SEQ ID NOS: 119 and 176. These exemplary FGFR-1 isoforms lack one or more domains or a part thereof compared to a cognate FGFR-1 such as set forth in SEQ ID NO:268. The exemplary FGFR-1 isoform set forth as SEQ ID NO: 119 contains immunoglobulin-like domain 2 between amino acids 67 – 157 and a portion of immunoglobulin-like domain 3 between amino acids 164 – 220. The exemplary FGFR-1 isoform set forth as SEQ ID NO: 176 contains immunoglobulin-like domain 2 between amino acids 70 – 159 and immunoglobulin-like domain 3 between amino acids 166 – 268. These exemplary isoforms each lack the transmembrane and protein kinase domains compared to a cognate FGFR-1 polypeptide (e.g. SEQ ID NO:268).

FGFR-1 isoforms, including FGFR-1 isoforms herein, can include allelic variation in the FGFR-1 polypeptide. For example, a FGFR-1 isoform can include one or more amino acid differences present in an allelic variant. In one example, a FGFR-1 isoform includes one or more allelic variation as set forth in SEQ ID NO:300. An allelic variant can include one or more amino acid change in the immunoglobulin domain, such as at positions corresponding to amino acid positions 97, 99, 165, 190, 192, and 198 of SEQ ID NO:268. An additional allelic variant can include one or more amino acid changes at a position corresponding to amino acid position 22 of SEQ ID NO:268.

b. FGFR-2

FGFR-2 is a member of the fibroblast growth factor receptor family. Ligands to FGFR-2 include a number of FGF proteins, such as, but not limited to, FGF-1 (basic FGF), FGF-2 (acidic FGF), FGF-4 and FGF-7. FGF receptors are involved in

cell-cell communication of tissue remodeling during development as well as cellular homeostasis in adult tissues. Overexpression of, or mutations in, FGFR-2 have been associated with hyperproliferative diseases, including a variety of human cancers, including breast, pancreatic, colorectal, bladder and cervical malignancies. FGFR-2 isoforms such as FGFR-2 intron fusion proteins can be used to treat conditions in which FGFR-2 is upregulated, including cancers.

The FGFR-2 protein (GenBank No. NP_000132 set forth as SEQ ID NO:269) is characterized by three immunoglobulin-like domains; domain 1 between amino acids 41 - 125, domain 2 between amino acids 159 – 249, and domain 3 between amino acids 256 – 360. FGFR-2 also contains a transmembrane domain between amino acids 378 – 400 and protein kinase domain between amino acids 481 – 757.

FGFR-2 proteins include allelic variants of FGFR-2. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:269. For example, one or more amino acid variations can occur in the immunoglobulin domain of FGFR-2. An allelic variant can include amino acid changes at position 105 where, for example Y can be replaced by C, or at position 162 where, for example, M can be replaced by T, or at position 172 where, for example, A can be replaced by F, or at position 186 (SNP NO: 755793) where, for example, M can be replaced by T, or at position 267 where, for example, S can be replaced by P, or at position 276 where, for example, F can be replaced by V, or at position 278 where, for example, C can be replaced by F, or at position 281 where, for example, Y can be replaced by C, or at position 289 where, for example, Q can be replaced by P, or at position 290 where, for example, W can be replaced by C, or at position 315 where, for example, A can be replaced by S, or at position 338 where, for example, G can be replaced by R, or at position 340 where, for example, Y can be replaced by H, or at position 341 where, for example, T can be replaced by P, or at position 342 where, for example, C can be replaced by R, Y, S, F, or W, or at position 344 where, for example, A can be replaced by P or G, or at position 347 where, for example, S can be replaced by C, or at position 351 where, for example, S can be replaced by C, or at position 354 where, for example, S can be replaced by C. Further examples of amino acid changes can occur in the transmembrane domain. An allelic variant can

include amino acid changes at position 384 where, for example, G can be replaced by R. Additional amino acid changes also can occur in the protein kinase domain. An allelic variant can include amino acid changes at position 549 where, for example, N can be replaced by H, or at position 565 where, for example, E can be replaced by G, or at position 641 where, for example, K can be replaced by R, or at position 659 where, for example, K can be replaced by N, or at position 663 where, for example, G can be replaced by E, or at position 678 where, for example, R can be replaced by G. Allelic variations also can occur at position 6 where, for example, R can be replaced by P, or at position 31 where, for example, T can be replaced by I, or at position 152 where, for example, R can be replaced by G, or at position 252 where, for example, S can be replaced by W or L, or at position 253 where, for example, P can be replaced by S or R, or at position 372 where, for example, S can be replaced by C, or at position 375 where, for example, Y can be replaced by C. In one example, an allelic variant includes one or more amino acid change compared to SEQ ID NO:269 and the variant exhibits a change in a biological activity. Amino acid changes occurring in the immunoglobulin domain, such as at positions 105, 172, 267, 276, 278, 281, 289, 290, 315, 338, 340, 341, 342, 344, 347, 351, 354, or the protein kinase domain, such as at positions 549, 565, 641, 659, 663, or 678, or other amino acid changes, such as at positions 252, 253, or 375, are associated with syndromic craniosynostosis including Apert, Crouzon, or Pfeiffer syndromes when such amino acid changes are present in a cognate FGFR-2 such as set forth in SEQ ID NO: 269. An exemplary FGFR-2 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 301.

Exemplary FGFR-2 isoforms include FGFR-2 isoforms set forth in SEQ ID NOS: 178, 180, 182 and 184. These exemplary FGFR-2 isoforms lack one or more domains or a part thereof compared to a cognate FGFR-2 such as set forth in SEQ ID NO:269. The exemplary FGFR-2 isoform set forth as SEQ ID NO: 184 contains three immunoglobulin-like domains; domain 1 between amino acids 41 – 125, domain 2 between amino acids 159 – 249 and domain 3 between amino acids 256 – 360, but lacks transmembrane and protein kinase domains. The exemplary FGFR-2 isoform set forth as SEQ ID NO: 180 contains the immunoglobulin-like domains 1, 2 and a

portion of domain 3 (between amino acids 41 – 125, 159 – 249 and 256 – 313, respectively), but is missing transmembrane and protein kinase domains. The exemplary FGFR-2 isoform set forth as SEQ ID NO: 178 contains immunoglobulin-like domain 1 between amino acids 41 – 125 and domain 2 between amino acids 159 – 249, but lacks immunoglobulin-like domain 3, and transmembrane and protein kinase domains. The exemplary FGFR-2 isoform set forth as SEQ ID NO: 182 contains immunoglobulin-like domains 2 between amino acids 44 – 134 and domain 3 between amino acids 141 – 245, but does not contain an immunoglobulin-like domain 1, a transmembrane domain and protein kinase domain.

FGFR-2 isoforms, including FGFR-2 isoforms herein, can include allelic variation in the FGFR-2 polypeptide. For example, a FGFR-2 isoform can include one or more amino acid differences present in an allelic variant. In one example, a FGFR-2 isoform includes one or more allelic variation as set forth in SEQ ID NO:301. An allelic variation can include one or more amino acid changes in the immunoglobulin domain, such as at positions 105, 162, 172, 186, 267, 276, 278, 281, 289, 290, 315, 338, 340, 341, 342, 344, 347, 351, or 354. Additional allelic variations can include one or more amino acid changes, such as at positions 6, 31, 152, 252, or 253.

c. FGFR-4

FGFR-4 is a member of the FGF receptor tyrosine kinase family. FGFR-4 regulation is modified in some cancer cells. For example, in some adenocarcinomas FGFR--4 is down-regulated compared with expression in normal fibroblast cells. Alternate forms of FGFR-4, are expressed in some tumor cells. For example, ptd-FGFR-4 lacks a portion of the FGFR-4 extracellular domain but contains the third Ig-like domain, a transmembrane domain and a kinase domain. This isoform is found in pituitary gland tumors and is tumorigenic. FGFR-4 isoforms can be used to treat diseases and conditions in which FGFR-4 is misregulated. For example, an FGFR-4-isoform can be used to down regulate tumorigenic FGFR-4 isoforms such as ptd-FGFR-4.

The FGFR-4 protein (GenBank No. NP_002002 set forth as SEQ ID NO: 271) is characterized by three immunoglobulin – like domains; domain 1 between amino

acids 35 – 113, domain 2 between amino acids 152 – 242, and domain 3 between amino acids 249 – 351. FGFR-4 also contains a transmembrane domain between amino acids 370 – 386 and protein kinase domain between amino acids 467 – 743.

FGFR-4 proteins include allelic variants of FGFR-4. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:271. For example, one or more amino acid variations can occur in the immunoglobulin domain of FGFR-4. An allelic variant can include amino acid changes at position 275 (SNP NO: 11954456) where, for example, S is replaced by R, or at position 297 (SNP NO:1057633) where, for example, D is replaced by V. Additional amino acid changes can occur in the protein kinase domain. An allelic variant can include an amino acid change at position 616 (SNP NO:2301344) where, for example, R can be replaced by L. Allelic variations also can occur at position 10 (SNP NO: 1966265) where, for example, V can be replaced by I, or at position 136 (SNP NO: 376618) where, for example, P can be replaced by L, or at position 388 (SNP NO: 351855) where, for example, G can be replaced by R. An exemplary FGFR-4 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 303.

Exemplary FGFR-4 isoforms lack one or more domains or a part thereof compared to a cognate FGFR-4 such as set forth in SEQ ID NO:271. Exemplary FGFR-4 isoforms include FGFR-4 isoforms set forth in SEQ ID NOS: 91, 109 and 121. The exemplary FGFR-4 isoform set forth as SEQ ID NO: 121 contains immunoglobulin-like domain 1 between amino acids 35 – 113, domain 2 between amino acids 152 – 242, and domain 3 between amino acids 249 – 351, but lacks a transmembrane and protein kinase domains. The exemplary FGFR-4 isoform set forth as SEQ ID NO: 109 contains immunoglobulin-like domain 2 between amino acids 62 – 154 and a portion of domain 3 between amino acids 161 – 209, but does not contain an immunoglobulin – like domain 1, a transmembrane and protein kinase domains. The exemplary FGFR-4 isoform set forth as SEQ ID NO: 91 lacks the immunoglobulin – like domains, the transmembrane domain and the protein kinase domain present in the cognate receptor (e.g. SEQ ID NO:271).

FGFR-4 isoforms, including FGFR-4 isoforms herein, can include allelic variation in the FGFR-4 polypeptide. For example, a FGFR-4 isoform can include one or more amino acid differences present in an allelic variant. In one example, a FGFR-4 isoform includes one or more allelic variation as set forth in SEQ ID NO:303. An allelic variation can include one or more amino acid changes in the immunoglobulin domain, such as at amino acids corresponding to positions 275 or 297 of SEQ ID NO:271. Additional allelic variants can include one or more amino acid changes, such as at amino acids corresponding to amino acid positions 10 or 136 of SEQ ID NO:271.

5. Platelet-Derived Growth Factor Receptors

Platelet-derived growth factor receptors (PDGFRs) are homo or heterodimers that contain two subunits, α and β. Receptor subunits are comprised of five Ig-like domains at the N-terminus, a transmembrane domain, and a split kinase domain at the C-terminus.

The PDGFR-A protein (GenBank No. NP_006197 set forth as SEQ ID NO: 275) is characterized by three immunoglobulin – like domains; domain 1 between amino acids 42 – 102, domain 2 between amino acids 228 – 292, and domain 3 between amino acids 319 – 412. PDGFR-A also contains a transmembrane domain between amino acids 527 – 549 and protein kinase domain between amino acids 593 – 953. The PDGFR-B protein (GenBank No. NP_002600 set forth as SEQ ID NO: 276) is characterized by two immunoglobulin – like domains between amino acids 32 – 119 and amino acids 213 – 311, a transmembrane domain between amino acids 534 – 556, and protein kinase domain between amino acids 600 – 958.

PDGF receptors can include allelic variation, for example, PDGFR-B and PDGFR-A allelic variants. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NOS:275 or 276. For example, with respect to PDGFR-B, allelic variations can include one or more amino acid change at position 29 (SNP NO:17110944) where, for example, I is replaced by F, or at position 194 (SNP NO:2229560) where, for example, I is replaced by T, or at position 345 (SNP NO:2229558) where, for example, P is replaced by S. An exemplary PDGFR-B

allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 307.

PDGF receptors and ligands are involved in a variety of cellular processes, including clot formation, extracellular matrix synthesis, chemotaxis of immune cells apoptosis and embryonic development. Overexpression of PDGF receptors has been linked to a number of human carcinomas, including stomach, pancreas, lung and prostate. Activation of the platelet derived growth factor receptor (PDGFR) is associated with benign prostatic hypertrophy and prostate cancer as well as other cancer types. Activation of PDGF-R also is associated with smooth muscle proliferation in development of atherosclerosis. PDGFR also has been implicated in modulating proliferative vitreoretinopathy, a common medical problem caused by the proliferation of fibroblastic cells behind the retina, resulting in retinal detachment. Similar to its receptor, PDGF ligand is a homo or heterodimer of A and/or B chains. The α-PDGF receptor can be activated by either PDGF-A or PDGF-B. A β-PDGF receptor only can be activated by the PDGF-B chain. Two additional members of the PDGF family also have been isolated, PDGF-C and PDGF-D.

Exemplary PDGFR isoforms include the isoforms set forth in SEQ ID NO:111 and 147. These exemplary PDGFR isoforms lack one or more domains or a part thereof compared to a cognate PDGFR such as set forth in SEQ ID NO:276. The exemplary PDGFR-A isoform set forth as SEQ ID NO: 111 is characterized by one immunoglobulin – like domains between amino acids 41 – 102, but does not contain a transmembrane domain or protein kinase domain. The exemplary PDGFR-B isoform set forth as SEQ ID NO: 147 is characterized by two immunoglobulin – like domains between amino acids 32 – 119 and amino acids 213 – 310, but does not contain transmembrane domain or protein kinase domain.

PDGFR isoforms, including PDGFR isoforms herein, can include allelic variation in the PDGFR polypeptide. For example, a PDGFR isoform can include one or more amino acid differences present in an allelic variant. In one example, a PDGFR isoform includes one or more allelic variation as set forth in SEQ ID NO:307. An allelic variation can include one or more amino acid changes, such as at amino acids corresponding to positions 29 or 194 of SEQ ID NO:276.

PDGFR isoforms can be used to target diseases and conditions in which PDGFR is involved, including hyperproliferative diseases, such as proliferative vitreoretinopathy and smooth muscle hyperproliferative conditions including atherosclerosis.

Flt3 (fms-related tyrosine kinase 3), CSF1R (colony stimulating factor 1 receptor) and KIT (receptor for c-kit) also are members of the PDGFR RTK subfamily. The CSF1R protein (GenBank No. NP_005202 set forth as SEQ ID NO: 249) is characterized by three immunoglobulin – like domains; domain 1 between amino acids 19 – 102, domain 2 between amino acids 202 – 324, and domain 3 between amino acids 412 – 487. CSF1R also is characterized by a transmembrane domain between amino acids 515 – 537 and protein kinase domain between amino acids 582 – 910. CSF1R proteins include allelic variants of CSF1R. In one example, an allelic variant contains one or more amino acid changes compared to a cognate CFS1R receptor such as set forth in SEQ ID NO:249. For example, one or more amino acid variations can occur in the immunoglobulin-like domain 2 of CSF1R. An allelic variant can include one or more amino acid changes as position 279 (SNP NO: 3829986) where, for example, V can be replaced by M. Allelic variants also can include amino acid changes at position 362 (SNP NO:10079250) where, for example, H can be replaced by R, or position 969 (SNP NO:1801271 where, for example, Y can be replaced by C. An exemplary CSF1R allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 285.

The exemplary CSF1R isoform set forth as SEQ ID NO: 145 contains an immunoglobulin – like domain 1 between amino acids 19 – 102, a partial immunoglobulin – like domain 2 between amino acids 202 – 296. SEQ ID NO: 145 does not contain Ig-like domain 3, a transmembrane or protein kinase domain. CSF1R isoforms, including CSF1R isoforms herein, can include allelic variation in the CSF1R polypeptide. For example, a CSF1R isoform can include one or more amino acid differences present in an allelic variant. In one example, a CSF1R isoform includes one or more allelic variation as set forth in SEQ ID NO:285. An allelic variation can include one or more amino acid changes in the immunoglobulin-like

domain 2, such as at positions 279. Allelic variations also can include one or more amino acid changes, such as at position 362.

The KIT receptor (GenBank No. NP_000213 set forth as SEQ ID NO:273) is characterized by an immunoglobulin – like domain between amino acids 210 – 336, a transmembrane domain between amino acids 521 – 543, and protein kinase domain between amino acids 589 – 924. KIT receptor include allelic variants of KIT. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:273, such as set forth in SEQ ID NO:305. For example, one or more amino acid variations can occur in the transmembrane domain of KIT. An allelic variant can include one or more amino acid changes at position 541 (SNP NO: 3822214)) where, for example, M can be replaced by L or V. Additional examples of amino acid changes can occur in the protein kinase domain. An allelic variant can include one or more amino acid changes at position 664 where, for example, G can be replaced by R, or at position 788 where, for example C can be replaced by R, or at position 801 where, for example, T can be replaced by I, or at position 816 where, for example, D can be replaced by V, H, or Y, or at position 820 where, for example, D is replaced by V, or at position 822 where, for example, N can be replaced by K or Y, or at position 823 where, for example, Y can be replaced by D or C, or at position 835 where, for example, W can be replaced by R, or at position 869 where, for example, P can be replaced by S, or at position 900 where, for example, Y can be replaced by F. Allelic variants also can include one or more amino acid change at position 52, where, for example, D is replaced by N, or at position 136 where, for example, C is replaced by R, or at position 178 where, for example, A is replaced by T, or at position 557 where, for example, W is replaced by R.

In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:273 and the variant exhibits a change in a biological activity. For example, an allelic variant contains one or more amino acid changes occurring in the protein kinase domain of KIT, such as at positions 816, 823, 822, or 801. In another example, one or more amino acid changes occur in the protein kinase domain, such as at position 900, and are associated with diminished receptor phosphorylation, association with adaptor proteins such as CrkII, and activation. In

the context of a wildtype or predominant form of the receptor such allelic variation can be associated with a disease or condition, for example, testicular seminomas, intracranial germinomas, chronic myelogenous leukemia, human peibaldism and idiopathic myelofibrosis.

The exemplary KIT isoform set forth as SEQ ID NO: 93 contains an immunoglobulin – like domain between amino acids 210 – 336, but does not contain a transmembrane domain or protein kinase domain. KIT isoforms, including KIT isoforms herein, can include allelic variation in the KIT polypeptide. For example, a KIT isoform can include one or more amino acid differences present in an allelic variant. In one example, a KIT isoform includes one or more allelic variations as set forth in SEQ ID NO:305. An allelic variation can include one or more amino acid changes, such as at amino acids corresponding to positions 136 or 178 of SEQ ID NO:273.

The Flt3 receptor (GenBank No. NP_004110 set forth as SEQ ID NO:272) is characterized by an immunoglobulin-like domain between amino acids 78 – 161 and between amino acids 257 – 345, a transmembrane domain between amino acids 542 – 564, and a tyrosine kinase domain between amino acids 610 – 943. Flt3 proteins include allelic variants of Flt3. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:272, such as those set forth in SEQ ID NO:304. For example, one or more amino acid variations can occur in the tyrosine kinase domain of Flt3. An allelic variant can include amino acid changes at position 835 where, for example, D can be replaced by Y, H, or F, or at position 836 where, for example, I can be replaced by S, or at position 841 where, for example, N can be replaced by I or Y, or at position 842 where, for example Y can be replaced by H. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:272 and the variant exhibits a change in a biological activity. One or more amino acid changes occurring in the tyrosine kinase domain of Flt3 receptor, such as at positions 835 or 841, can result in the constitutive activation of downstream targets of Flt3, such as signal transducer and activator of transcription STAT5, in the absence of Flt3 ligand stimulation. One or more amino acid changes can be present in the tyrosine kinase domain of Flt3, such as at positions 835, 836,

and 842, also can be associated with a disease or condition, for example the progression from myelodysplastic syndrome to acute myeloid leukemia in infants and adults.

Flt3 is expressed in placenta and various adult tissues such as gonads, brain and in hematopoietic cells. Flt3 is associated with biological regulation in gonads, brain and nervous systems. Flt3 has been implicated as a target for pediatric cancers such as pediatric AML. KIT is involved in regulation in a broad variety of cell types including erythroid cells, interstitial cells, mast cells and germ cells. KIT is associated with a variety of cancers including gastrointestinal stromal tumors. RTK isoforms of Flt3, CSF1R and KIT can be used in the treatment of diseases and conditions in which the RTK are involved.

6. MET (Receptor for hepatocye growth factor)

MET is a RTK for hepatocyte growth factor (HGF), a multifunctional cytokine controlling cell growth, morphogenesis and motility. HGF, a paracrine factor produced primarily by mesenchymal cells, induces mitogenic and morphogenic changes, including rapid membrane ruffling, formation of microspikes, and increased cellular motility. Signaling through MET can increase tumorigenicity, induce cell motility and enhance invasiveness *in vitro* and metastasis *in vivo*. MET signaling also can increase the production of protease and urokinase, leading to extracellular matrix/basal membrane degradation, which are important for promoting tumor metastasis.

MET is a RTK that is highly expressed in hepatocytes. MET is comprised of two disulfide-linked subunit, a 50-kD α subunit and a 145-kD β subunit. In the fully processed MET protein, the α subunit is extracellular, and the β subunit has extracellular, transmembrane, and tyrosine kinase domains. The ligand for MET is hepatocyte growth factor (HGF). Signaling through FGF and MET stimulates mitogenic activity in hepatocytes and epithelial cells, including cell growth, motility and invasion. As with other RTKs, these properties link MET to oncogenic activities. In addition to a role in cancer, MET also has been shown to be a critical factor in the development of malaria infection. Activation of MET is required to make

hepatocytes susceptible to infection by malaria, thus MET is a prime target for prevention of the disease.

The MET receptor (GenBank No. NP_000236 set forth as SEQ ID NO:274) is characterized by a Sema domain between amino acids 55 – 500. In addition to hepatocyte growth factor receptor, the Sema domain occurs in semaphorins, which are a large family of secreted and transmembrane proteins, some of which function as repellent signals during axon guidance. In MET, the Sema domain has been shown to be involved in receptor dimerization in addition to ligand binding. The MET protein also is characterized by a plexin cysteine rich repeat between amino acids 519 – 562, three IPT/TIG domains between amino acids 563 – 655, amino acids 657 – 739 and amino acids 742 – 836. IPT stands for **I**mmunoglobulin-like fold shared by **P**lexins and **T**ranscription factors. TIG stands for the Immunoglobulin-like domain in transcription factors (**T**ranscription factor **IG**). TIG domains in MET likely play a role in mediating some of the interactions between extracellular matrix and receptor signaling. The MET protein also is characterized by a transmembrane domain between amino acids 951 – 973 and cytoplasmic protein kinase domain between amino acids 1078 – 1337.

MET receptors include allelic variants of MET. In one example, an allelic variant contains one or more amino acid changes compared to SEQ ID NO:274. For example, one or more amino acid variations can occur in the Sema domain of MET. An allelic variant can include amino acid changes at position 113 where, for example, K is replaced by R, or at position 114 where, for example, D is replaced by N, or at position 145 where, for example, V is replaced by A, or at position 148 where, for example, H is replaced by R, or at position 151 where, for example, T is replaced by P, or at position 158 where, for example, V is replaced by A, or at position 168 where, for example, E is replaced by D, or at position 193 where, for example, I is replaced by T, or at position 216 where, for example, V is replaced by L, or at position 237 where, for example, V is replaced by A, or at position 276 where, for example, T is replaced by A, or at position 314 where, for example, F is replaced by L, or at position 337 where, for example, L is replaced by P, or at position 340 where, for example, D is replaced by V, or at position 382 where, for example, N is replaced by

D, or at position 400 where, for example, R is replaced by G, or at position 476 where, for example, H is replaced by R, or at position 481 where, for example, L is replaced by M, or at position 500 where, for example, D is replaced by G. In a further example, one or more amino acid variation can occur in the plexin cysteine rich repeat domain of MET. An allelic variant can include amino acid changes at position 542 where, for example, H can be replaced by Y. In other examples, one or more amino acid variation can occur in the IPT/TIG domains of MET. An allelic variant can include amino acid changes at position 622 where, for example, L is replaced by S, or at position 720 where, for example, F is replaced by S, or at position 729 where, for example, A is replaced by T. In an additional example, one or more amino acid variations can occur in the protein kinase domain of MET. An allelic variant can include amino acid changes at position 1094 where, for example, H is replaced by R or at position 1100 where, for example, N is replaced by Y or at position 1230 where, for example, Y is replaced by C, or at position 1235 where, for example, Y is replaced with D, or at position 1250 where, for example, M is replaced by T. Allelic variants also can include one or more amino acid changes, such as at position 37 where, for example, V is replaced by A, or at position 39 where, for example M is replaced by T, or at position 42 where, for example, Q is replaced by R, or at position 501 where, for example, Y can be replaced by H, or at position 511 where, for example, T can be replaced by A. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:274 and the variant exhibits a change in a biological activity. An exemplary MET allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 306. Amino acid changes occurring in the tyrosine kinase domain of MET receptor, such as those described above, can be associated with dysregulated function of MET. For example, in the context of a wildtype or predominant form of the receptor, allelic changes in MET receptor are implicated in the development of human cancer including the promotion of tumor invasion, angiogenesis, and metastasis.

Exemplary isoforms of MET provided herein lack one or more domains or a part thereof compared to a cognate MET receptor such as set forth in SEQ ID NO:274. Exemplary MET receptor isoforms provided herein (*e.g.* SEQ ID NOS:

103, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, and 214) lack a transmembrane domain and/or a protein kinase domain. In addition, exemplary MET isoforms provided herein contain one or more domains of a wildtype or predominant form of MET receptor (e.g. set forth as SEQ ID NO:274). For example, MET receptor isoforms set forth as SEQ ID NOS: 103, 190, 192, 196, 198, 200, 202, 204, 206, 208, 210, 212, and 214 all contain complete Sema domains. MET isoforms set forth as SEQ ID NOS: 103, 192, 196, 198, 200, 202, 206, 208, 210, 212, and 214 contain complete plexin cysteine rich repeat domains. Met receptor isoforms can include one or more IPT/TIG domains. For example, MET receptor isoforms set forth as SEQ ID NOS: 103, 198, 200, 202, 204, 206, 208, 210, 212, and 214 contain at least one complete IPT/TIG domain. MET receptor isoforms set forth as SEQ ID NOS: 103, 208, 210, 212, and 214 all contain at least two complete IPT/TIG domains. MET receptor isoforms set forth as SEQ ID NOS: 103 and 212 contain three complete IPT/TIG domains. Among the MET receptor isoforms provided herein are isoforms that contain a portion of a domain compared to a wildtype or predominant form of MET receptor (e.g. set forth as SEQ ID NO:274). For example, MET receptor isoforms set forth as SEQ ID NOS: 186, 188, and 194 contain portions of the Sema domain between amino acids 55 – 412, 55 – 468, and 55 – 400, respectively. The MET receptor isoform set forth as SEQ ID NO: 196 contains a portion of an IPT/TIG domain between amino acids 563 – 621. MET receptor isoforms set forth as SEQ ID NOS: 198, 200 and 204, in addition to the one full IPT/TIG domain, contain a portion of a second IPT/TIG domain (between amino acids 657 – 664, 657 – 719, and 629 – 672, respectively). The MET receptor isoform set forth as SEQ ID NO: 210, in addition to the two full IPT/TIG domains, contains a portion of a third IPT/TIG domain between amino acids 742 – 823.

MET isoforms, including MET isoforms herein, can include allelic variation in the MET polypeptide. For example, a MET isoform can include one or more amino acid differences present in an allelic variant. In one example, a MET isoform includes one or more allelic variations as set forth in SEQ ID NO:306. An allelic variation can include one or more amino acid change in the Sema domain, such as at positions 113, 114, 145, 148, 151, 158, 168, 193, 216, 237, 276, 314, 337, 340, 382, 400, 476, 481,

481, or 500. Allelic variations also can occur in the plexin cysteine rich repeat domain, such as at position 542. Further allelic variations also can occur in the IPT/TIG domain, such as at positions 622, 720, or 729. Allelic variations also can include other amino acid changes, such as at positions 37, 39, 42, 501, or 511.

MET isoforms can be used in treating or preventing metastatic cancer, and in inhibiting angiogenesis, such as angiogenesis necessary for tumor growth. Therapeutic applications of MET isoforms include lung cancer, malignant peripheral nerve sheath tumors (MPNST), colon cancer, gastric cancer, and cutaneous malignant melanoma.

MET isoforms also can be used in combination with other anti-angiogenesis drugs to prevent tumor cell invasiveness. Anti-angiogenesis drugs produce a state of hypoxia in tumors which can promote tumor cell invasion by sensitizing cells to HGF stimulation. MET isoforms can target and modulate biological activity of MET, such as by inhibiting or down-regulating MET when, anti-angiogenesis drugs are given, thus preventing or inhibiting tumor cell invasiveness.

Therapeutic applications of MET isoforms also include prevention of malaria. Plasmodium, the causative agent of malaria, must first infect hepatocytes to initiate a mammalian infection. Sporozoites migrate through several hepatocytes, by breaching their plasma membranes, before infection is finally established in one of them. Wounding of hepatocytes by sporozoite migration induces the secretion of hepatocyte growth factor (HGF), which renders hepatocytes susceptible to infection. Infection depends on activation of the HGF receptor, MET, by secreted HGF. The malaria parasite exploits MET as a mediator of signals that make the host cell susceptible to infection. HGF/MET signaling induces rearrangements of the host-cell actin cytoskeleton that are required for the early development of the parasites within hepatocytes. MET- isoforms can be administered as a therapeutic to downregulate MET, thus inhibiting or preventing induction of MET signaling by malaria parasite and therefore inhibiting or preventing malaria infection.

RON (recepteur d'origine nantais; also known as macrophage stimulating 1 receptor) is another member of the MET subfamily of RTKs. A ligand for RON is macrophage-stimulating protein (MSP). RON is expressed in cells of epithelial

origin. RON plays a role in epithelial cancers including lung cancer and colon cancers. RON and MET are expressed in ovarian cancers and are suggested to confer a selective advantage to cancer cells, thus promoting cancer progression. RON also is overexpressed in certain colorectal cancers. Germline mutations in the RON gene have been linked to human tumorigenesis. RON isoforms can be used to modulate RON, such as by modulating RON activity in diseases and conditions where RON is overexpressed.

The RON protein (GenBank No. NP_002438 set forth as SEQ ID NO:277) is characterized by a Sema domain between amino acids 58 – 507, a plexin cysteine rich domain between amino acids 526 – 568, three IPT/TIG domains (between amino acids 569 – 671, amino acids 684 – 767, and amino acids 770 – 860), a transmembrane domain between amino acids 960 – 982 and cytoplasmic protein kinase domain between amino acids 1082 – 1341.

RON receptors include allelic variants of RON. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO:277, such as those set forth in SEQ ID NO:308. For example, one or more amino acid variations can occur in the Sema domain of RON. An allelic variant can include single nucleotide polymorphisms (SNP) at position 113 (SNP No. 3733136) where, for example, G is replaced by S, or at position 209 where, for example, G is replaced by A, or at position 322 (SNP No. 2230593) where, for example, Q is replaced by R, or at position 440 (SNP No. 2230592) where, for example, N is replaced by S. An amino acid variation also can occur at position 523 (SNP No. 2230590) where, for example, R is replaced by Q, or at position 946 (SNP No. 13078735) where, for example V is replaced by M. Additionally, one or more amino acid variations can occur in the protein kinase domain of RON. An allelic variant can include amino acid changes at position 1195 (SNP No. 7433231) where, for example, G is replaced by S, or at position 1335 (SNP No. 1062633) where, for example, R is replaced by G, or at position 1232 where, for example, D is replaced by V, or at position 1254 where, for example, M is replaced by T. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:277 and the variant exhibits a change in a biological activity. Allelic variants, for example in the context of a wildtype or

predominant form of the receptor, can be associated with a disease or condition. For example, amino acid changes occurring in the tyrosine kinase domain of RON, such as at positions corresponding to 1232 and 1254 of SEQ ID NO:277, can be associated with oncogenic cell transformation and tumor development by causing cellular accumulation of b-catenin whereby increases in the levels of b-catenin are associated with cancer.

SEQ ID NOS: 129, 216, 218 and 220 set forth exemplary RON isoforms. Exemplary RON isoforms lack one or more domains or a part thereof compared to a cognate RON such as set forth in SEQ ID NO:277. For example, exemplary RON isoforms set forth as SEQ ID NOS: 129, 216, 218 and 220 lack a transmembrane domain and protein kinase domain. The exemplary RON isoform set forth as SEQ ID NO:129 is characterized by a truncated Sema domain between amino acids 58 – 495. SEQ ID NO: 129 does not contain the plexin cysteine rich domain and IPT/TIG domains. The exemplary RON isoform set forth as SEQ ID NO: 216 also is characterized by a truncated Sema domain between amino acids 58 – 410, a complete plexin cysteine rich domain between amino acids 420 – 462, and a portion of an IPT/TIG domain between amino acids 463 – 521. The exemplary RON isoform set forth as SEQ ID NO: 220 contains complete Sema and plexin cysteine rich domains as well as a portion of an IPT/TIG domain between amino acids 569 – 627. SEQ ID NO: 218 sets forth an exemplary RON isoform that contains a complete Sema domain, plexin cysteine rich domain, and three IPT/TIG domains.

RON isoforms, including RON isoforms herein, also can include allelic variation in the RON polypeptide. For example a RON isoform can include one or more amino acid differences present in an allelic variant. In one example, a RON isoform includes one or more allelic variations as set forth in SEQ ID NO:308. An allelic variant can include one or more amino acid changes in the Sema domain, such as at positions 113, 209, 322. or 440. An allelic variant also can include one or more amino acid change, such as at position 523.

7. Vascular endothelial growth factor (VEGF)

The vascular endothelial growth factor (VEGF) is a family of closely related growth factors with a conserved pattern of eight cysteine residues and sharing

common VEGF receptors. VEGF receptors include VEGFR-1 (Flt-1) VEGFR-2 (Flk-1/KDR), and VEGFR-3 (Flt-4). Ligands for VEGF receptors include vascular endothelial growth factor-A (also known as vasculotropin (VAS) or vascular permeability factor (VPF)) VEGF-B, VEGF-C, VEGF-D and placental growth factor (PlGF). The VEGF proteins and receptors play an important role in many aspects of angiogenesis, including cell migration, proliferation and tube formation, thus linking these proteins to the pathogenesis of many types of cancer. Flt-1, Flk, and Flt-4/KDR are genes encoding VEGFR family members.

Exemplary RTK- isoforms for targeting VEGFR-related diseases and conditions include VEGFR isoforms set forth in SEQ ID NOS: 99-102, 110, 123, 125, 127, 224 and 226. Such isoforms can be used in the treatment of acute inflammatory disease, such as Kawasaki disease, rheumatoid arthritis, diabetic retinopathy, retinopathy and psoriasis, as well as re-regulation of abnormal angiogenesis. Additionally VEGFR- isoforms can be used for treatment of cancers including breast carcinoma.

a. VEGFR-1 (Flt-1)

Flt-1 (*fms*-like tyrosine kinase-1) is a member of the VEGF receptor family of tyrosine kinases. Ligands for Flt-1 include VEGF-A and PlGF (placental growth factor). Since Flt-1 and its ligands are important for angiogenesis, disregulation of these proteins have significant impacts on a variety of diseases stemming from abnormal angiogenesis, such as proliferation or metastasis of solid tumors, rheumatoid arthritis, diabetic retinopathy, retinopathy and psoriasis. Flt-1 also has been implicated in Kawasaki disease, a systemic vasculitis with microvascular hyperpermeability.

The VEGFR-1 polypeptide set forth as SEQ ID NO:282 (GenBank No. NP_002010) is characterized by four immunoglobulin – like domains; domain 1 between amino acids 231 – 337, domain 2 between 332 – 427, domain 3 between amino acids 558 – 656, and domain 4 between amino acids 661 – 749. VEGR-1 also contains a transmembrane domain between amino acids 764 – 780 and protein kinase domain between amino acids 827 – 1154.

SEQ ID NOS: 99-102, 110 and 123 set forth exemplary VEGFR-1 isoforms. The exemplary VEGFR-1 isoforms lack one or more domains or a part thereof compared to a cognate VEGFR-1 such as set forth in SEQ ID NO:282. For example, the exemplary VEGFR-1 isoforms lack a transmembrane domain and protein kinase domain compared to a cognate VEGFR-1 (e.g. SEQ ID NO:282). Such isoforms also can lack additional domains or portions of domains of a cognate VEGFR-1. The exemplary VEGFR-1 isoforms set forth as SEQ ID NOS: 99, 100 and 110 contain two immunoglobulin – like domains between amino acids 231 – 337 and between amino acids 332 – 427, but do not contain immunoglobulin-like domains 2 and 3. The exemplary VEGFR-1 isoform set forth as SEQ ID NO: 101 contains immunoglobulin – like domain 1 between amino acids 231 – 337 and a portion of immunoglobulin – like domain 2 between amino acids 332 – 394. The exemplary VEGFR-1 isoform set forth as SEQ ID NO: 102 contains a portion of one immunoglobulin – like domain between amino acids 231 – 331. VEGFR-1 isoforms, including VEGFR-1 isoforms herein, can include allelic variation in the VEGFR-1 polypeptide, such as one or more amino acid changes compared to a cognate VEGFR-1 polypeptide (e.g., SEQ ID NO: 282).

b. VEGFR-2 (KDR/Flk-1)

VEGFR-2 (KDR/Flk-1) is a member of the VEGF receptor family of tyrosine kinases. Ligands for VEGFR-2 includes VEGF. VEGF interacts with its receptors, VEGFR-2 and VEGFR-1, expressed on endothelial and hematopoietic stem cells, and thereby promotes recruitment of these cells to neo-angiogenic sites, accelerating the revascularization process. As such, VEGF is found in several types of tumors and has a tumoral angiogenic activity *in vitro* and *in vivo*. The interaction of VEGF with VEGFR-1 mediates cell migration whereas the interaction of VEGF with VEGFR-2 mediates cell proliferation. The VEGFR-2 receptor is the main human receptor responsible for the VEGF activity in physiological and pathological vascular development, and VEGF-KDR signaling pathway is a potential target for the development of anti- and pro- angiogenic agents.

The VEGFR-2 protein (GenBank No. NP_002244 set forth as SEQ ID NO:283) is characterized by three immunoglobulin – like domains; domain 1 between

amino acids 224 – 325, domain 2 between amino acids 333 – 418, and domain 3 between amino acids 666 – 766. VEGFR-2 also contains a transmembrane domain between amino acids 763 – 785 and protein kinase domain between amino acids 834 – 1160.

VEGFR-2 proteins include allelic variants of VEGFR-2. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 283. For example, one or more amino acid variations can occur in the immunoglobulin-like domain of VEGFR-2. An allelic variant can include single nucleotide polymorphisms (SNP) at position 297 (SNP No: 2305948) where, for example, V can be replaced by I, or at position 349 (SNP No: 1824302) where, for example, R can be replaced by K, or at position 392 (SNP No: 2034964) where, for example, D can be replaced by N. Additionally, one or more amino acid variations can occur in the protein kinase domain of VEGFR-2. An allelic variant can include amino acid changes at position 835 (SNP No: 1139775) where, for example, K is replaced by N, or at position 848 (SNP No: 1139776) where, for example, V is replaced by E, or at position 952 (SNP No: 13129474) where, for example, V is replaced by I. One or more amino acid changes also can occur in the transmembrane domain. An allelic variant can include amino acid changes at position 772 (SNP No: 1062832) where, for example A is replaced by T. An amino acid variation also can occur at position 472 (SNP No: 1870377) where, for example, Q is replaced by H, or at position 787 (SNP No: 1139774) where, for example, R is replaced by G, or at position 1147 where, for example, P is replaced by S, or at position 1210 (SNP No: 11540507) where, for example, P is replaced by I, or at position 1347 (SNP No: 1139777) where, for example, S is replaced by T. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:283 and the variant exhibits a change in biological activity. Allelic variants, for example in the context of a wildtype or predominant form of the receptor, can be associated with a disease or condition. For example, amino acid changes occurring in the kinase domain of VEGFR-2, such as at position 1147 described herein, can be associated with tumors such as those found in Juvenile hemangiomas. An exemplary VEGFR-2

allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 313.

Exemplary isoforms of VEGFR-2 include isoforms lacking one or more domains or a part thereof compared to a cognate VEGFR-2 such as set forth in SEQ ID NO:283. Such isoforms include the isoform set forth in SEQ ID NO: 224 that does not contain transmembrane or protein kinase domains. The exemplary VEGFR-2 isoform set forth as SEQ ID NO:224 is characterized by immunoglobulin – like domains between amino acids 224 – 325, amino acids 333 – 418, and a portion of a third immunoglobulin – like domain between amino acids 666 – 691.

VEGFR-2 isoforms, including VEGFR-2 isoforms herein, can include allelic variation in the VEGFR-2 polypeptide. For example a VEGFR-2 isoform can include one or more amino acid differences present in an allelic variant. In one example, a VEGFR-2 isoform includes one or more allelic variations as set forth in SEQ ID NO:313. An allelic variant can include one or more amino acid changes in the immunoglobulin-like domain, such as at positions 297, 349, or 392. Allelic variants also can include one or more amino acid change such as at position 472.

c. VEGFR-3

VEGFR-3 is expressed predominantly in lymphatic endothelial cells. VEGFR-3 signaling is crucial for development and maintenance of lymphatic vessels. Mouse models expressing VEGFR-3 can be used to assess effects on lymphatic tissue development and maintenance in the presence of VEGFR-3 isoforms. VEGFR-3 also can have effects on blood vascular endothelium.

The VEGFR-3 polypeptide (GenBank No. NP_002011 set forth as SEQ ID NO:284) is characterized by four immunoglobulin – like domains; domain 1 between amino acids 231 – 328, domain 2 between amino acids 349 – 398, domain 3 between amino acids 571 – 655 and domain 4 between amino acids 677 – 766. VEGFR-3 also contains a transmembrane domain between amino acids 776 – 798 and protein kinase domain between amino acids 845 – 1169.

VEGFR-3 polypeptides include allelic variants of VEGFR-3. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 284. For example, one or more amino acid variations can occur in the protein kinase

domain of VEGFR-3. An allelic variant can include single nucleotide polymorphisms (SNP) at position 854 where, for example, G can be replaced by S, or at position 890 (SNP No: 448012) where, for example, Q can be replaced by H, or at position 915 where, for example, A can be replaced by P, or at position 916 where, for example, C and be replaced by W, or at position 933 where, for example, G can be replaced by R, or at position 954 where, for example, P can be replaced by S, or at position 1008 where, for example, P can be replaced by L, or at position 1041 where, for example, R can be replaced by W or Q, or at position 1137 where, for example, P can be replaced by L, or at position 1164 (SNP No: 1049080) where, for example, D can be replaced by E. An amino acid variation also can occur at position 24 where, for example, D is replaced by G, or at position 134 where, for example, D is replaced by G, or at position 149 where, for example, N can be replaced by D, or at position 494 (SNP No: 307826) where, for example T can be replaced by A, or at position 1189 (SNP No: 744282) where, for example, R can be replaced by C. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:284 and the variant exhibits a change in a biological activity. Amino acid changes occurring in the tyrosine kinase domain can interfere with VEGFR-3 signaling, such as those described herein at positions 854, 915,916, 933, 1041, and 1137. Allelic variants, for example in the context of a wildtype or predominant form of the receptor can be associated with a disease or condition. For example, amino acid changes occurring in the tyrosine kinase domain can be associated with primary congenital lymphoedema; amino acid changes at position 954 can be associated with tumors such as juvenile hemangiomas. An exemplary VEGFR-3 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 314.

Exemplary VEGFR-3 isoforms lack one or more domains or a part thereof compared to a cognate VEGFR-3 such as set forth in SEQ ID NO:284. SEQ ID NOS: 125, 127 and 226 set forth exemplary VEGFR-3 isoforms that lack a transmembrane and protein kinase domains. Such isoforms contain other domains of VEGFR-3. The exemplary VEGFR-3 isoform set forth as SEQ ID NO:226 is characterized by immunoglobulin – like domain 1 between amino acids 231 – 328, domain 2 between amino acids 349 – 398, domain 3 between amino acids 571 – 655, and a portion of a

domain 4 between amino acids 677 – 723. SEQ ID NO: 127 is characterized by one immunoglobulin – like domain between amino acids 231 – 272.

VEGFR-3 isoforms, including VEGFR-3 isoforms herein, also can include allelic variation in the VEGFR-3 polypeptide compared to a cognate VEGFR-3 receptor such as set forth in SEQ ID NO:284. For example a VEGFR-3 isoform can include one or more amino acid differences present in an allelic variant such as set forth in SEQ ID NO:314, for example at positions corresponding to amino acid position 24, 134, 149 or 494 of SEQ ID NO:284.

8. TIE

Tie-1 and Tie-2/TEK (tyrosine kinase with immunoglobulin-like and EGF-like domains) receptors are endothelial RTKs with immunoglobulin and epidermal growth factor homology domains. Exemplary RTK- isoforms for targeting Tie/TEK receptors include RTK isoforms set forth in SEQ ID NO: 104, 105, 112, 113, 131, 133, 135, 137, 139, 141, 143 and 222. Such RTK isoforms can be used for treatment of diseases and conditions in which the Tie/Tek receptor is implicated, including anti-angiogenesis therapy in diseases such as cancer, eye diseases, and rheumatoid arthritis. Other diseases and conditions that can be treated with TIE/TEK isoforms include inflammatory diseases such as arthritis, rheumatism, and psoriasis, benign tumors and preneoplastic conditions, myocardial angiogenesis, hemophilic joints, scleroderma, vascular adhesions, atherosclerotic plaque neovascularization, telangiectasia, and wound granulation. Additional targets for TEK receptor isoforms include diseases in which TEK is overexpressed, for example, chronic myeloid leukemia.

a. Tie-1

Tie-1 is a receptor tyrosine kinase that plays an essential role in vascular development and angiogenesis where it is thought to be required for vessel maturation and stabilization. Tie-1 also acts as an antiapoptotic survival signal. Tie-1 expression is associated with endothelial cells and neovascularization and physically associates with the related receptor TEK. Tie-1 also is expressed in a variety of tumors and metastases including lung and breast and also is involved in thyroid

tumorigenesis. Tie-1 is strongly induced during wound healing. The ligands responsible for activating Tie-1 remain unidentified.

The Tie-1 receptor set forth as SEQ ID NO:279 (GenBank No. NP_005415 set forth as SEQ ID NO: 279) is characterized by two immunoglobulin domains between amino acids 139 – 197 and amino acids 365 – 428, an EGF domain between amino acids 224 – 255, a laminin EGF-like domain between amino acids 231 – 272, three fibronectin type III domains (between amino acids 446 – 533, amino acids 546 – 632, and amino acids 644 – 729), transmembrane domain between amino acids 764 – 786, and cytoplasmic protein kinase domain between 839 – 1107.

Tie-1 proteins include allelic variants of Tie-1. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 279. For example, one or more amino acid variations can occur in the immunoglobulin domain of Tie-1. An allelic variant can include single nucleotide polymorphisms (SNP) at position 142 (SNP No: 11545380) where, for example, A can be replaced by T. An amino acid variation also can occur at position 1109 (SNP No: 6698998) where, for example, R is replaced by C. An exemplary Tie-1 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 310.

Exemplary Tie-1 isoforms lack one or more domains or a part thereof compared to a cognate Tie-1 such as set forth in SEQ ID NO:279. For example, the exemplary Tie-1 isoforms provided herein lack transmembrane and protein kinase domains. Such exemplary Tie-1 isoforms include the Tie-1 isoforms set forth in SEQ ID NOS:113, 135, 137, 139, 141, 143 and 222. These isoforms contain other domains of the Tie-1 receptor. The exemplary Tie-1 isoform set forth as SEQ ID NOS: 113 and 222 are characterized by two immunoglobulin domains between amino acids 139 – 197 and amino acids 365 – 428, an EGF domain between amino acids 224 – 255, a laminin EGF-like domain between amino acids 231 – 272, and three fibronectin type III domains (between amino acids 446 – 533, amino acids 546 – 632, and amino acids 644 – 729). The exemplary Tie-1 isoforms set forth as SEQ ID NOS: 137, 141 and 143 contain an immunoglobulin domain between amino acids 139 – 197, an EGF domain between amino acids 224 – 255 and a laminin EGF-like domain between

amino acids 231 – 272. The exemplary Tie-1 isoforms set forth as SEQ ID NOS: 135 and 139 contain at least a portion of the immunoglobulin domain.

Tie-1 isoforms, including Tie-1 isoforms herein, can include allelic variation in the Tie-1 polypeptide. For example, a Tie-1 isoform can include one or more amino acid differences compared to a cognate Tie-1 receptor (e.g. SEQ ID NO:279). In one example, a Tie-1 isoform includes one or more allelic variations as set forth in SEQ ID NO:310. For example, an allelic variant of a Tie-1 isoform can include an amino acid change in the immunoglobulin domain, such as at position 142.

b. Tie-2 (TEK)

The known ligands for Tie-2/TEK include angiopoietin (Ang)-1 and Ang-2. These RTKs play an important role in the development of the embryonic vasculature and continue to be expressed in adult endothelial cells. Tie-2/TEK is a RTK that is expressed almost exclusively by vascular endothelium. Expression of Tie-2/TEK is important for the development of the embryonic vasculature. Overexpression and/or mutation of Tie-2/TEK has been linked to pathogenic angiogenesis, and thus tumor growth, as well as myeloid leukemia.

The Tie-2/TEK protein (GenBank No. NP_000450 set forth as SEQ ID NO:278) is characterized by a laminin EGF-like domain between amino acids 219 – 268, three fibronectin type III domains (between amino acids 444 – 529, amino acids 543 – 626, and amino acids 639 – 724), a transmembrane domain between amino acids 748 – 770, and cytoplasmic protein kinase domain between amino acids 824 – 1092.

TEK proteins include allelic variants of TEK. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 278. For example, one or more amino acid variations can occur in fibronectin type III domain of TEK. An allelic variant can include single nucleotide polymorphisms (SNP) at position 486 (SNP No: 1334811) where, for example, V can be replaced by I, or at position 695 where, for example, I can be replaced by T, or at position 724 (SNP No. 4631561) where, for example, A can be replaced by T. An allelic variant also can occur in the protein kinase domain of TEK. An allelic variant can include amino acid changes at position 849 where, for example, R can be replaced by W. An amino acid

variation also can occur at position 346 where, for example, P can be replaced by Q. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:278 and the variant exhibits a change in a biological activity. Allelic variants, for example in the context of a wildtype or predominant form of the receptor can be associated with a disease or condition. For example, amino acid changes occurring in the kinase domain of TEK receptor, such as at position 849, can be associated with vascular dysmorphogenesis due to increased activity of TEK. An exemplary TEK allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 309.

Exemplary Tie-2/TEK isoforms lack one or more domains or a part thereof compared to a cognate TEK such as set forth in SEQ ID NO:278. For example, exemplary TEK isoforms set forth in SEQ ID NO: 104, 105, 112, 131 and 133 lack a transmembrane domain and kinase domain. Tie-2/TEK isoforms can contain other domains of a Tie-2/TEK cognate receptor.. The exemplary TEK isoforms set forth as SEQ ID NO: 104 contains a laminin EGF – like domain between amino acids 219 – 268 and three fibronectin type III domains between amino acids 401 – 486, amino acids 500 – 580, and amino acids 593 - 678. The exemplary TEK isoforms set forth as SEQ ID NO: 105 contains a laminin EGF – like domain between amino acids 219 – 268 and three fibronectin type III domains between amino acids 444 – 529, amino acids 543 – 623, and amino acids 636 – 721. The exemplary TEK isoforms set forth as SEQ ID NO: 112 contains a laminin EGF – like domain between amino acids 196 – 245 and three fibronectin type III domains between amino acids 378 – 463, amino acids 477 – 557, and amino acids 570 – 655. The exemplary TEK isoform set forth as SEQ ID NO: 131 contains a laminin EGF-like domain between amino acids 219 – 268, but is missing the three fibronectin type III domains. The exemplary TEK isoform set forth as SEQ ID NO: 133 contains a laminin EGF-like domain between amino acids 219 – 268 and a portion of a fibronectin type III domain between amino acids 444 – 497.

TEK isoforms, including TEK isoforms herein, can include allelic variation in the TEK polypeptide. For example, a TEK isoform can include one or more amino acid differences present in an allelic variant. In one example, a TEK isoform

includes one or more allelic variations as set forth in SEQ ID NO:309. An allelic variant can include one or more amino acid change in the fibronectin type III domain, such as at position 486 or 695. An allelic variant also can include one or more amino acid change, such as at position 346.

9. Tumor Necrosis Factor Receptors (TNFRs)

The TNF (tumor necrosis factor) ligand and receptor family regulate a variety of signal transduction pathways including those involved in cell differentiation, activation, and viability. TNFRs have a characteristic repeating extracellular cysteine-rich motif and a variable intracellular domain that differs between members of the TNFR family. The TNFR family of receptors includes, but is not limited to, TNFR1, TNFR2, TNFRrp, the low-affinity nerve growth factor receptor, Fas antigen, CD40, CD27, CD30, 4-1BB, OX40, DR3, DR4, DR5, and herpesvirus entry mediator (HVEM). Ligands for TNFRs include TNF- α, lymphotoxin, nerve growth factor, Fas ligand, CD40 ligand, CD27 ligand, CD30 ligand, 4-1BB ligand, OX40 ligand, APO3 ligand, TRAIL and LIGHT. TNFRs include an extracellular domain, including a ligand binding domain, a transmembrane domain and an intracellular domain that participates in signal transduction. Additionally, TNFRs are typically trimeric proteins that trimerize at the cell surface. Trimerization is important for biological activity of TNFRs.

TNF plays a key role in inflammatory and infectious diseases. TNF binds two receptors, TNF-R1 and TNF-R2 that can transduce intracellular signals when expressed on the cell surface. TNFR1 is a major mediator of biological signaling involved in cell apoptosis, cytotoxicity, fibroblast proliferation, synthesis of prostaglandin E2 and resistance to Chlamydia. TNFR2 is involved in proliferation of thermocytes, TNF-dependent proliferative response to mononuclear cells, induction of GM-CSF secretion, inhibition of early hematopoiesis, and down-regulating activated T cells by inducing apoptosis. TNFR1 and TNFR2 also are produced as soluble forms by proteolytic cleavage (sTNFR). Increased levels of sTNFRs have been found in inflammatory and infectious diseases.

TNF/TNFRs are targets for many viruses. Viruses can bind to and sequester host cytokines, such as TNF, thus allowing the virus to escape the immune system.

Many viruses encode proteins that mimic TNFR by binding TNF or that are viral homologs of TNFR. Viruses can upregulate TNF gene activity and/or expression, modulate TNF/TNFR effects, and bind to TNFR. TNFR isoforms, such as described herein, can be used to modulate TNFRs, including viral TNFR homologs and mimics. Examples of viruses that interact with TNF/TNFRs and are targets for TNFR isoforms include, but are not limited to, DNA viruses including Myxoma virus, Vaccinia virus, Tanapox virus, Epstein-Barr virus, Herpes simplex virus, Cytomegalovirus, Herpesvirus saimiri, Hepatitis B virus, African swine fever virus and Parovirus, and RNA viruses including Human Immune deficiency virus (HIV), Hepatitis C virus, Influenza virus, Respiratory syncytial virus, Measles virus, Vesicular stomatitis virus, Dengue virus and Ebola virus (see for example, Herbein *et al.* (2000) *Proc Soc Exp Biol Med. 223(3)*:241-57). Exemplary TNFR isoforms include isoforms of TNFR1 such as set forth in SEQ ID NO: 95.

a. TNFR1

The TNFR1 polypeptide set forth as SEQ ID NO:280 (GenBank No. NP_001056) is characterized by three TNFR c6 domains (between amino acids 44 – 81, amino acids 84 – 125, and amino acids 127 – 166), a transmembrane domain between amino acids 212 – 234, and a death domain between amino acids 357 – 441 within the cytoplasmic tail. The TNFR c6 domains are cysteine-rich domains at the N-terminal region that can be subdivided into repeats containing six conserved cysteines, all of which are involved in intrachain disulfide bonds. Death domains are characteristic of the TNFR1 receptor family and are involved in initiating apoptosis and NF-κB and other signaling pathways upon ligand binding.

TNFR1 polypeptides include allelic variants of TNFR1. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 280. For example, one or more amino acid variations can occur in the c6 domains of TNFR2. An allelic variant can include single nucleotide polymorphisms (SNP) at position 75 (SNP No: 4149637) where, for example, P can be replaced by I, or at position 121 (SNP No. 4149584) where, for example, R can be replaced by Q. An amino acid variation also can occur at position 305 where, for example, P can be

replaced by T. An exemplary TNFR1 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 311.

b. TNFR2

TNFR2 (GenBank No. NP_001057 set forth as SEQ ID NO:281) is characterized by three TNFR c6 domains between amino acids 40 – 75, amino acids 78 – 118 and amino acids 120 – 161 and a transmembrane domain between amino acids 258 – 280. TNFR2 proteins include allelic variants of TNFR2. In one example, an allelic variant contains one or more amino acids changes compared to SEQ ID NO: 281. For example, one or more amino acid variations can occur in the transmembrane domain. An allelic variant can include single nucleotide polymorphisms at position 295 (SNP No: 5746032) where, for example, Q can be replaced by R. An amino acid variation also can occur at position 187 (SNP No: 5746025) where, for example, V can be replaced by M, or at position 196 (SNP No: 1061622) where, for example, M can be replaced by R, or at position 232 (SNP No: 5746026) where, for example, E can be replaced by K, or at position 236 (SNP No: 5746027) where, for example, A can be replaced by T, or at position 264 (SNP No: 5746031) where, for example, L can be replaced by P. In one example, an allelic variant includes one or more amino acid changes compared to SEQ ID NO:281 and the variant exhibits a change in a biological activity. Allelic variants, for example in the context of a wildtype or predominant form of the receptor can be associated with a disease or condition. For example, amino acid changes occurring at position 196, for example, can be associated with autoimmune disease such as rheumatoid arthritis and acute graft-versus-host disease and diseases associated with polycystic ovary syndrome and hyperandrogenism. An exemplary TNFR2 allelic variant containing one or more amino acid changes described above is set forth as SEQ ID NO: 312.

Exemplary TNFR2 isoforms lack one or more domains or a part thereof compared to a cognate TNFR2 such as set forth in SEQ ID NO:281. The exemplary TNFR2 isoform set forth as SEQ ID NO:95 lacks a transmembrane domain. Additionally, this isoform is characterized by TNFR c6 domains between amino acids 40 – 75 and amino acids 78 – 118 as well as a portion of a third c6 domain between amino acids 120 – 152.

G. Methods of Producing Nucleic Acid Encoding CSR Isoforms and Methods of Producing CSR isoform Polypeptides

Exemplary methods for generating CSR isoform nucleic acid molecules and polypeptides are provided herein. Such methods include *in vitro* synthesis methods for nucleic acid molecules such as PCR, synthetic gene construction and *in vitro* ligation of isolated and/or synthesized nucleic acid fragments. CSR isoform nucleic acid molecules also can be isolated by cloning methods, including PCR of RNA and DNA isolated from cells and screening of nucleic acid molecule libraries by hybridization and/or expression screening methods.

CSR isoform polypeptides can be generated from CSR isoform nucleic acid molecules using *in vitro* and *in vivo* synthesis methods. CSR isoforms can be expressed in any organism suitable to produce the required amounts and forms of isoform 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. CSR isoforms also can be isolated from cells and organisms in which they are expressed, including cells and organisms in which isoforms are produced recombinantly and those in which isoforms are synthesized without recombinant means such as genomically-encoded isoforms produced by alternative splicing events.

1. Synthetic genes and polypeptides

CSR isoform nucleic acid molecules and polypeptides can be synthesized by methods known to one of skill in the art using synthetic gene synthesis. In such methods, a polypeptide of a CSR isoform is "back-translated" to generate one or more nucleic acid molecules encoding an isoform. The back-translated nucleic acid molecule is then synthesized as one or more DNA fragments such as by using automated DNA synthesis technology. The fragments are then operatively linked to form a nucleic acid molecule encoding an isoform. Nucleic acid molecules also can be joined with additional nucleic acid molecules such as vectors, regulatory sequences for regulating transcription and translation and other polypeptide-encoding nucleic acid molecules. Isoform-encoding nucleic acid molecules also can be joined with labels such as for tracking, including radiolabels, and fluorescent moieties.

The process of backtranslation uses the genetic code to obtain a nucleotide gene sequence for any polypeptide of interest, such as a CSR isoform. The genetic code is degenerate, 64 codons specify 20 amino acids and 3 stop codons. Such degeneracy permits flexibility in nucleic acid design and generation, allowing for example restriction sites to be added to facilitate the linking of nucleic acid fragments and the placement of unique identifier sequences within each synthesized fragment. Degeneracy of the genetic code also allows the design of nucleic acid molecules to avoid unwanted nucleotide sequences, including unwanted restriction sites, splicing donor or acceptor sites, or other nucleotide sequences potentially detrimental to efficient translation. Additionally, organisms sometimes favor particular codon usage and/or a defined ratio of GC to AT nucleotides. Thus, degeneracy of the genetic code permits design of nucleic acid molecules tailored for expression in particular organisms or groups of organisms. Additionally, nucleic acid molecules can be designed for different levels of expression based on optimizing (or non-optimizing) of the sequences. Back-translation is performed by selecting codons that encode a polypeptide. Such processes can be performed manually using a table of the genetic code and a polypeptide. Alternatively, computer programs, including publicly available software can be used to generate back-translated nucleic acid sequences.

To synthesize a back-translated nucleic acid molecule, any method available in the art for nucleic acid synthesis can be used. For example, individual oligonucleotides corresponding to fragments of a CSR isoform-encoding sequence of nucleotides are synthesized by standard automated methods and mixed together in an annealing or hybridization reaction. Such oligonucleotides synthesized by such annealing result in the self-assembly of the gene from the oligonucleotides using overlapping single-stranded overhangs formed upon duplexing complementary sequences, generally about 100 nucleotides in length. Single nucleotide "nicks" in the duplex DNA are sealed using ligation, for example with bacteriophage T4 DNA ligase. Restriction endonuclease linker sequences can for example, then be used to insert the synthetic gene into any one of a variety of recombinant DNA vectors suitable for protein expression. In another, similar method, a series of overlapping oligonucleotides are prepared by chemical oligonucleotide synthesis methods.

Annealing of these oligonucleotides results in a gapped DNA structure. DNA synthesis catalyzed by enzymes such as DNA polymerase I can be used to fill in these gaps, and ligation is used to seal any nicks in the duplex structure. PCR and/or other DNA amplification techniques can be applied to amplify the formed linear DNA duplex.

Additional nucleotide sequences can be joined to a CSR isoform-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 an isoform-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 isoform-encoding nucleic acid molecules. Such regions include, but are not limited to, sequences to facilitate uptake of an isoform into specific target cells, or otherwise enhance the pharmacokinetics of the synthetic gene.

CSR isoforms also can be synthesized using automated synthetic polypeptide synthesis. Cloned and/or *in silico*-generated polypeptides can be synthesized in fragments and then chemically linked. Alternatively, isoforms can be synthesized as a single polypeptide. Such polypeptides then can be used in the assays and treatment administrations described herein.

2. Methods of cloning and isolating CSR isoforms

CSR isoforms 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 an isoform, including for example, polymerase chain reaction (PCR) methods. A nucleic acid containing material can be used as a starting material

from which an isoform -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 an isoform. For example, primers can be designed based on expressed sequences from which an isoform is generated. Primers can be designed based on back-translation of an isoform amino acid sequence. Nucleic acid molecules generated by amplification can be sequenced and confirmed to encode an isoform.

Nucleic acid molecules encoding isoforms also can be isolated using library screening. For example, a nucleic acid library representing expressed RNA transcripts as cDNA molecules can be screened by hybridization with nucleic acid molecules encoding CSR isoforms or portions thereof. For example, an intron sequence or portion thereof from a CSR gene can be used to screen for intron retention containing molecules based on hybridization to homologous sequences. Expression library screening can be used to isolate nucleic acid molecules encoding a CSR isoform. For example, an expression library can be screened with antibodies that recognize a specific isoform or a portion of an isoform. Antibodies can be obtained and/or prepared which specifically bind to a CSR isoform or a region or peptide contained in an isoform. Antibodies which specifically bind to an isoform can be used to screen an expression library containing nucleic acid molecules encoding an isoform, such as an intron fusion protein. Methods of preparing and isolating antibodies, including polyclonal and monoclonal antibodies and fragments therefrom are well known in the art. Methods of preparing and isolating recombinant and synthetic antibodies also are well known in the art. For example, such antibodies can be constructed using solid phase peptide synthesis or can be produced recombinantly, using nucleotide and amino acid sequence information of the antigen binding sites of antibodies that specifically bind to a candidate polypeptide. Antibodies also can be obtained by screening combinatorial libraries containing variable heavy chains and variable light chains, or antigen-binding portions thereof. Methods of preparing, isolating and using polyclonal, monoclonal and non-natural antibodies are reviewed,

for example, in Kontermann and Dubel, eds. (2001) "Antibody Engineering" Springer Verlag; Howard and Bethell, eds. (2001) "Basic Methods in Antibody Production and Characterization" CRC Press; and O'Brien and Aitkin, eds. (2001) "Antibody Phage Display" Humana Press. Such antibodies also can be used to screen for the presence of an isoform polypeptide, for example, to detect the expression of a CSR isoform in a cell, tissue or extract.

3. Synthetic isoforms

A variety of synthetic forms of the isoforms are provided. Included among them are conjugates in which the isoform or intron-encoded portion thereof is linked directly or via linker to another agent, such as a targeting agent or to a molecule the present or provides the intron-encoded portion or isoform portion to the CSR so that an activity of the CSR is modulated. Other synthetic forms include chimeras in which the extracellular domain portion and C-terminal portion, such as an intron-encoded portion, are from different isoforms. Also provided are "peptidomimetic" isoforms in which one or more bonds in the peptide backbone is (are) replaced by a bioisotere or other bond such that the resulting polypeptide peptidomimetic has improved properties, such as resistance to proteases, compared to the unmodified form

a. Isoform conjugates

CSR isoforms also can be provided as conjugates between the isoform and another agent. The conjugate can be used to target to a receptor with which the isoform interacts and/or to another targeted receptor for delivery of isoform. Such conjugates include linkage of a CSR isoform to a targeted agent and/or targeting agent. Conjugates can be produced by any suitable method including chemical conjugation or by expression of fusion proteins in which, for example, DNA encoding a targeted agent or targeting agent, with or without a linker region, is operatively linked to DNA encoding an RTK isoform. Conjugates also can be produced by chemical coupling, typically through disulfide bonds between cysteine residues present in or added to the components, or through amide bonds or other suitable bonds. Ionic or other linkages also are contemplated.

Pharmaceutical compositions can be prepared that contain CSR isoform conjugates and treatment effected by administering a therapeutically effective amount

of a conjugate, for example, in a physiologically acceptable excipient. CSR isoform conjugates also can be used in *in vivo* therapy methods such as by delivering a vector containing a nucleic acid encoding a CSR isoform conjugate as a fusion protein.

Conjugates can contain one or more CSR isoforms linked, either directly or via a linker, to one or more targeted agents: (CSR isoform)n, (L)q, and (targeted agent)m in which at least one CSR isoform is linked directly or via one or more linkers (L) to at least one targeted agent. Such conjugates also can be produced with any portion of a CSR isoform sufficient to bind to a target, such as a target cell type for treatment. Any suitable association among the elements of the conjugate and any number of elements where n, and m are integer greater than 1 and q is zero or any integer greater then 1, is contemplated as long as the resulting conjugates interacts with a targeted CSR or targeted cell type.

Examples of a targeted agent include drugs and other cytotoxic molecules such as toxins that act at or via the cell surface and those that act intracellularly. Examples of such moieties, include radionuclides, radioactive atoms that decay to deliver, *e.g.*, ionizing alpha particles or beta particles, or X-rays or gamma rays, that can be targeted when coupled to a CSR isoform. Other examples include chemotherapeutics that can be targeted by coupling with an isoform. For example, geldanamycin targets proteosomes. An isoform-geldanamycin molecule can be directed to intracellular proteosomes, degrading the targeted isoform and liberating geldanamycin at the proteosome. Other toxic molecules include toxins, such as ricin, saporin and natural products from conches or other members of phylum mollusca. Another example of a conjugate with a targeted agent is a CSR isoform coupled, for example as a protein fusion, with an antibody or antibody fragment. For example, an isoform can be coupled to an Fc fragment of an antibody that binds to a specific cell surface marker to induce killer T cell activity in neutrophils, natural killer cells, and macrophages. A variety of toxins are well known to those of skill in the art.

Conjugates can contain one or more CSR isoforms linked, either directly or via a linker, to one or more targeting agents: (CSR isoform)n, (L)q, and (targeting agent)m in which at least one CSR isoform is linked directly or via one or more linkers (L) to at least one targeting agent. Any suitable association among the

elements of the conjugate and any number of elements where n, and m are integer greater than 1 and q is zero or any integer greater then 1, is contemplated as long as the resulting conjugates interacts with a target, such as a targeted cell type.

Targeting agents include any molecule that targets a CSR isoform to a target such as a particular tissue or cell type or organ. Examples of targeting agents include cell surface antigens, cell surface receptors, proteins, lipids and carbohydrate moieties on the cell surface or within the cell membrane, molecules processed on the cell surface, secreted and other extracellular molecules. Molecules useful as targeting agents include, but are not limited to, an organic compound; inorganic compound; metal complex; receptor; enzyme; antibody; protein; nucleic acid; peptide nucleic acid; DNA; RNA; polynucleotide; oligonucleotide; oligosaccharide; lipid; lipoprotein; amino acid; peptide; polypeptide; peptidomimetic; carbohydrate; cofactor; drug; prodrug; lectin; sugar; glycoprotein; biomolecule; macromolecule; biopolymer; polymer; and other such biological materials. Exemplary molecules useful as targeting agents include ligands for receptors, such as proteinaceous and small molecule ligands, and antibodies and binding proteins, such as antigen-binding proteins.

Alternatively, the CSR isoform, which specifically interacts with a particular receptor (or receptors) is the targeting agent and it is linked to targeted agent, such as a toxin, drug or nucleic acid molecule. The nucleic acid molecule can be transcribed and/or translated in the targeted cell or it can be regulatory nucleic acid molecule.

The CSR and be linked directly to the targeted (or targeting agent) or via a linker. Linkers include peptide and non-peptide linkers and can be selected for functionality, such as to relieve or decrease stearic hindrance caused by proximity of a targeted agent or targeting agent to a CSR isoform and/or increase or alter other properties of the conjugate, such as the specificity, toxicity, solubility, serum stability and/or intracellular availability and/or to increase the flexibility of the linkage between a CSR isoform and a targeted agent or targeting agent. Examples of linkers and conjugation methods are known in the art (see, for example, WO 00/04926). CSRs also can be targeted using liposomes and other such moieties that direct delivery of encapsulated or entrapped molecules.

b. Chimeric and synthetic intron fusion polypeptides

Also provided are chimeric and synthetic intron fusion polypeptides. These contain an intron from an intron fusion polypeptide operatively linked at the N-terminus to another polypeptide or other molecule such that the resulting molecule modulates the activity of a CSR, particularly an RTK, including any involved in pathways that participate in the inflammatory response, angiogenesis, neovascularization and/or cell proliferation. Included among these synthetic "polypeptides" are chimeric intron fusion polypeptides in which the N-terminus from the extracellular domain of a CSR is linked to the intron of an intron fusion protein, such as intron 8 of a herstatin (see, *e.g.*, SEQ ID Nos. 320-359). Exemplary herstatins are set forth in SEQ ID Nos. 320-359. Table 3A below identifies the sequences. Other herstatin variants include allelic variants, particularly those with variation in the extracellular domain portion.

Table 3A

Variant	Encoded Intron 8	SEQ ID NO (nucleotide)	SEQ ID NO (amino acid)
Herstatin prominent	AA: 341-419		320
Intron 8 prominent- molecule in a bottle			321
Herstatin variant (AA 342: Thr or Ser)	AA: 341-419		322
Herstatin variant (AA 345: Leu or Pro	AA: 341-419		323
Herstatin variant (AA 346: Pro or Leu)	AA: 341-419		324
Herstatin variant (AA 356: Leu or Gln)	AA 341-419		325
Herstatin variant (AA 358: Met or Leu)	AA 341-419		326
Herstatin variant (AA 361: Gly, Asp, Ala, or Val)	AA 341-419		327
Herstatin variant (AA 376: Leu or Ile)	AA 341-419		328
Herstatin variant (AA 394: Pro or Arg)	AA 341-419		329
Herstatin variant (AA 404: Pro or Leu)	AA 341-419		330
Herstatin variant (AA 413: Asp or Asn)	AA 341-419		331
Herstatin variant (AA 357: Arg or Cys)	AA 341-419		332
Herstatin variant (AA 371: Arg or Ile)	AA 341-419		333
Intron 8 variant (AA 2: Thr or Ser)			334
Intron 8 variant (AA 5: Leu or Pro)			335
Intron 8 variant (AA 6: Pro or Leu)			336
Intron 8 variant (AA 16: Leu or Gln)			337
Intron 8 variant (AA 18: Met or Leu)			338
Intron 8 variant (AA 21: Gly, Asp, Ala, or Val)			339
Intron 8 variant (AA 36: Leu or Ile)			340
Intron 8 variant (AA 54: Pro or Arg)			341
Intron 8 variant (AA 64: Pro or Leu)			342
Intron 8 variant (AA 73: Asp or Asn)			343
Intron 8 variant (AA 17: Arg or Cys)			344
Intron 8 variant (AA 31: Arg or Ile)			345
Intron 8 prominent- molecule in a bottle		346	
Intron 8 variant (nt 4: n= T)		347	
Intron 8 variant (nt 14: n= C)		348	
Intron 8 variant (nt: 17: n= T)		349	
Intron 8 variant (nt 47= A)		350	
Intron 8 variant (nt 54= A)		351	
Intron 8 variant (nt 62: n= C,T, A)		352	
Intron 8 variant (nt 106= A)		353	
Intron 8 variant (nt 161= G)		354	
Intron 8 variant (nt 191: n= T)		355	
Intron 8 variant (nt 217: C)		356	
Intron 8 variant (nt 17: n= T and nt 217: n= C)		357	
Intron 8 variant (nt 49: n=T)		358	
Intron 8 variant (nt 92: n=T)		359	

The N-terminus portion can be linked to a C-terminus (intron-encoded portion) of the synthetic intron fusion protein directly or via a linker, such as a polypeptide linker or a chemical linker. Linkage can be effected by recombinant expression of a fusion protein where there is no linker or where the linker is a polypeptide. Chemical synthesis also can be employed. When the linker is not a polypeptide, linkage can be effected chemically.

Any suitable linker can be selected so long as the resulting molecule interacts with a CSR and modulates, typically inhibits, its activity. Linkers can be selected to add a desirable property, such as to increase serum stability, solubility and/or intracellular concentration and to reduce steric hindrance caused by close proximity when one or more linkers is(are) inserted between the N-terminal portion and intron-encoded portion. The resulting molecule is designed or selected to retain the ability to modulate the activity of a CSR, particularly RTKs, including any involved in pathways that are involved in inflammatory responses, neovascularization, angiogenesis and cell proliferation.

Linkers include chemical linkers and peptide linkers, such as peptides that increase flexibility or solubility of the linked moieties, and chemical linkers. For example linkers can be inserted using heterobifunctional reagents, such as those described below, or, can be linked by linking DNA encoding polypeptide linker to the DNA encoding the N-terminal (and/or C-terminal portion) and expressing the resulting chimera. In addition, where no linker is present the N-terminus can be linked directly to the intron encoded portion. In some embodiments, the N-terminus portion can be replaced by non-peptidic moiety that provides sufficient steric hindrance and bulk to permit the intron-encoded portion to interact with and modulate the activity of a receptor. As noted above, the N-terminus also can be selected to target the intron-encoded portion to selected CSRs or a selected CSR.

Exemplary linkers include, but are not limited to, (Gly4Ser)n, (Ser4Gly)n and (AlaAlaProAla)n (see, SEQ ID NO: 319) in which n is 1 to 4, such as 1, 2, 3 or 4, such as:

(1) Gly4Ser with NcoI ends SEQ ID NO. 315

CCATGGGCGG CGGCGGCTCT GCCATGG

(2) (Gly4Ser)2 with NcoI ends SEQ ID NO. 316

CCATGGGCGG CGGCGGCTCT GGCGGCGGCG GCTCTGCCAT GG

(3) (Ser4Gly)4 with NcoI ends SEQ ID NO. 317

CCATGGCCTC GTCGTCGTCG GGCTCGTCGT CGTCGGGCTC

GTCGTCGTCG GGCTCGTCGT CGTCGGGCGC CATGG

(4) (Ser4Gly)2 with NcoI ends SEQ ID NO. 318

CCATGGCCTC GTCGTCGTCG GGCTCGTCGT CGTCGGGCGC CATGG

(5) (AlaAlaProAla)n, where n is 1 to 4, such as 2 or 3 (see, SEQ ID NO.:319)

c. Heterobifunctional cross-linking reagents

Numerous heterobifunctional cross-linking reagents that are used to form covalent bonds between amino groups and thiol groups and to introduce thiol groups into proteins, are known to those of skill in this art (see, e.g., the PIERCE CATALOG, ImmunoTechnology Catalog & Handbook, 1992-1993, which describes the preparation of and use of such reagents and provides a commercial source for such reagents; see, also, e.g., Cumber et al. (1992) Bioconjugate Chem. 3:397-401; Thorpe et al. (1987) Cancer Res. 47:5924-5931; Gordon et al. (1987) Proc. Natl. Acad Sci. 84:308-312; Walden et al. (1986) J. Mol. Cell Immunol. 2:191-197; Carlsson et al. (1978) Biochem. J. 173: 723-737; Mahan et al. 91987) Anal. Biochem. 162:163-170; Wawryznaczak et al. (1992) Br. J. Cancer 66:361-366; Fattom et al. (1992) Infection & Immun. 60:584-589). These reagents may be used to form covalent bonds between the N-terminal portion and C-terminus intron-encoded portion or between each of those portions and a linker. These reagents include, but are not limited to: N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP; disulfide linker); sulfosuccinimidyl 6-[3-(2-pyridyldithio)propion¬amido]hexanoate (sulfo-LC-SPDP); succinimidyloxycarbonyl-α-methyl benzyl thiosulfate (SMBT, hindered disulfate linker); succinimidyl 6-[3-(2-pyridyldithio) propionami¬do]¬hexanoate (LC-SPDP); sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC); succinimi¬dyl 3-(2-pyridyldithio)butyrate (SPDB; hindered disulfide bond linker); sulfosuccinimidyl 2-(7-azido-4-methylcoumarin-3-acetamide) ethyl-1,3'-dithiopropionate (SAED); sulfo-succinimidyl 7-azido-4-methylcoumarin-3-acetate (SAMCA); sulfosuccinimidyl-6-[alpha-methyl-alpha-(2-pyridyldithio)toluamido]-

hexanoate (sulfo-LC-SMPT); 1,4-di-[3'-(2'-pyridyldithio)propion-amido]butane (DPDPB); 4-succinimidyloxycarbonyl-α-methyl-α-(2-pyridylthio)toluene (SMPT, hindered disulfate linker);sulfosuccinimidyl-6-[α-methyl-α-(2-pyrimiyldi-thio)toluamido]hexanoate (sulfo-LC-SMPT); m-maleimidobenzoyl-N-hydroxy-succinimide ester (MBS); m-maleimidobenzoyl-N-hydroxysulfo-succinimide ester (sulfo-MBS); N-succinimidyl(4-iodoacetyl)aminobenzoate (SIAB; thioether linker); sulfosuccinimidyl-(4-iodoacetyl)amino benzoate (sulfo-SIAB); succinimidyl-4-(p-maleimi-dophenyl)butyrate (SMPB); sulfosuccinimidyl4-(p-maleimido-phenyl)buty-rate (sulfo-SMPB); azidobenzoyl hydrazide (ABH). These linkers, for example, can be used in combination with peptide linkers, such as those that increase flexibility or solubility or that provide for or eliminate steric hindrance. Any other linkers known to those of skill in the art for linking a polypeptide molecule to another molecule can be employed. General properties are such that the resulting molecule is biocompatible (for administration to animals, including humans) and such that the resulting molecule modulates the activity of a CSR.

4. Expression Systems

CSR isoforms, including natural and combinatorial intron fusion proteins, can be produced by any method known to those of skill in the art including *in vivo* and *in vitro* methods. CSR isoforms can be expressed in any organism suitable to produce the required amounts and forms of CSR isoforms 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 CSR isoforms. 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.

CSR isoforms also can be utilized or expressed as protein fusions. For example, an isoform fusion can be generated to add additional functionality to an isoform. Examples of isoform 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.

a. Prokaryotic expression

Prokaryotes, especially *E.coli*, provide a system for producing large amounts of proteins such as CSR isoforms. Transformation of *E.coli* is simple and rapid technique well known to those of skill in the art. Expression vectors for *E.co*li 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.

Isoforms 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 CSR isoforms 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 CSR isoforms. 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 adeninivoran*s 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 CSR isoforms. 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 unip*uncta (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 alb*opictus) 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 CSR isoforms. 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 that are 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 used to express CSR isoforms. 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 syntase 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 CSR isoforms (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 CSR isoforms produced in these hosts.

5. Engineered CSR isoforms

CSR isoforms can be designed and produced with one or more modified properties. These properties include but are not limited to increased protein stability, such as an increased protein half-life, increased thermal tolerance and/or resistance to one or more proteases. For example, a CSR isoform can be modified to increase protein stability *in vitro* and/or *in vivo*. *In vivo* stability can include protein stability under particular administration conditions such as stability in blood, saliva, and/or digestive fluids.

a. Modified proteins

CSR isoforms can be modified using any methods known in the art for modification of proteins. Such methods include site-directed and random mutagenesis. Non-natural amino acids and/or non-natural covalent bonds between amino acids of the polypeptide can be introduced into a CSR isoform to increase protein stability. In such modified CSR isoforms, the biological function of the isoform can remain unchanged compared to the unmodified isoform. Assays such as the assays for biological function provided herein and known in the art can be used to assess the biological function of a modified CSR isoform

b. Peptidomimetic isoforms.

Also provided are "peptidomimetic" isoforms in which one or more bonds in the peptide backbone (or other bond(s)) is (are) replaced by a bioisotere or other bond such that the resulting polypeptide peptidomimetic has improved properties, such as resistance to proteases, compared to the unmodified form.

H. Assays to assess or monitor isoform activities or affects on CSR Activities

CSR isoforms can exhibit alterations in structure or in one more activities compared to a full-length, wildtype or predominant form of a receptor. In addition, the CSR isoforms can alter (modulate) the activity of a CSR. All such isoforms are candidate therapeutics.

Where the isoforms exhibits a difference in an activity, *in vitro* and *in vivo* assays can be used to monitor or screen CSR isoforms. *In vitro* and *in vivo* assays also can be used to screen CSR isoforms to identify or select those that modulate the activity of a particular receptor or pathway. Such assays are well known to those of skill in the art. One of skill in the art can test a particular isoform for interaction with a CSR or a CSR ligand and/or test to assess any change in activity compared to a CSR. Some are exemplified herein.

Exemplary *in vitro* and *in vivo* assays are provided herein for comparison of an activity of an RTK isoform to an activity of a wildtype or predominant form of an RTK. Many of the assays are applicable to other CSRs and CSR isoforms. In addition, numerous assays, such as assays for kinase activities and cell proliferation activities of CSRs are known to one of skill in the art. Assays for activities of RTK isoforms and RTKs include, but are not limited to, kinase assays, homodimerization and heterodimerization assays, protein:protein interaction assays, structural assays, cell signaling assays and *in vivo* phenotyping assays. Assays also include employing animal models, including disease models in which an activity can be observed and/or measured or otherwise assessed. Dose response curves of a CSR isoform in such assays can be used to assess modulation of biological activities and as well as to determine therapeutically effective amounts of a CSR isoform for administration. Assays for RTK isoforms and RTKs include, but are not limited to, kinase assays, homodimerization and heterodimerization assays, protein:protein interaction assays, structural assays, cell signaling assays and *in vivo* phenotyping assays. Assays for TNFRs include, but are not limited, trimerization assays, localization assays such as membrane localization assays, protein:protein interaction assays, structural assays, cell signaling assays and *in vivo* phenotyping assays. Exemplary assays are described below.

1. Kinase assays

Kinase activity can be detected and/or measured directly and indirectly. For example, antibodies against phosphotyrosine can be used to detect phosphorylation of an RTK, RTK isoform, an RTK:RTK isoform complex and phosphorylation of other proteins and signaling molecules. For example, activation of tyrosine kinase activity of an RTK can be measured in the presence of a ligand for an RTK. Transphosphorylation can be detected by anti-phosphotyrosine antibodies. Transphosphorylation can be measured and/or detected in the presence and absence of an RTK isoform, thus measuring the ability of an RTK isoform to modulate the transphosphorylation of an RTK. Briefly, cells expressing an RTK isoform or that have been exposed to an RTK isoform, are treated with ligand. Cells are lysed and protein extracts (whole cell extracts or fractionated extracts) are loaded onto a polyacrylamide gel, separated by electrophoresis and transferred to membrane, such as used for western blotting. Immunoprecipitation with anti-RTK antibodies also can be used to fractionate and isolate RTK proteins before performing gel electrophoresis and western blotting. The membranes can be probed with anti-phosphotyrosine antibodies to detect phosphorylation as well as probed with anti-RTK antibodies to detect total RTK protein. Control cells, such as cells not expressing RTK isoform and cells not exposed to ligand can be subjected to the same procedures for comparison.

Tyrosine phosphorylation also can be measured directly, such as by mass spectroscopy. For example, the effect of an RTK isoform on the phosphorylation state of an RTK can be measured, such as by treating intact cells with various concentrations of an RTK isoform and measuring the effect on activation of an RTK. The RTK can be isolated by immunoprecipitation and trypsinized to produce peptide fragments for analysis by mass spectroscopy. Peptide mass spectroscopy is a well-established method for quantitatively determining the extent of tyrosine phosphorylation for proteins; phosphorylation of tyrosine increases the mass of the peptide ion containing the phosphotyrosine, and this peptide is readily separated from the non-phosphorylated peptide by mass spectroscopy.

For example, tyrosine-1139 and tyrosine-1248 are known to be autophosphorylated in the ErbB2 RTK. Trypsinized peptides can be empirically

determined or predicted based on polypeptide, for example by using ExPASy-PeptideMass program. The extent of phosphorylation of tyrosine-1139 and tyrosine-1248 can be determined from the mass spectroscopy data of peptides containing these tyrosines. Such assays can be used to assess the extent of auto-phosphorylation of an RTK isoform and the ability of an RTK isoform to transphosphorylate an RTK.

2. Complexation

Complexation, such as dimerization of RTKs and RTK isoforms and trimerization of TNFRs and TNFR isoforms, can be detected and/or measured. For example, isolated polypeptides can be mixed together, subjected to gel electrophoresis and western blotting. CSRs and/or CSR isoforms also can be added to cells and cell extracts, such as whole cell or fractionated extracts, and can be subjected to gel electrophoresis and western blotting. Antibodies recognizing the polypeptides can be used to detect the presence of monomers, dimers and other complexed forms. Alternatively, labeled CSRs and/or labeled CSR isoforms can be detected in the assays.

For example, such assays can be used to compare homodimerization of an RTK or heterodimerization of two or more RTKs in the presence and absence of an RTK isoform. Assays also can be performed to assess homodimerization of an RTK isoform and/or its ability to heterodimerize with an RTK. For example an ErbB2 RTK isoform can be assessed for its ability to heterodimerize with ErbB2, ErbB3 and ErbB4. Additionally, an ErbB2 RTK isoform can be assessed for its ability to modulate the ability of ErbB2 to homodimerize with itself.

3. Ligand binding

Generally, CSRs bind to one or more ligands. Ligand binding modulates the activity of the receptor and thus modulates, for example, signaling within a signal transduction pathway. Ligand binding of a CSR isoform and ligand binding of a CSR in the presence of a CSR isoform can be measured. For example, labeled ligand such as radiolabeled ligand can be added to purified or partially purified CSR in the presence and absence (control) of a CSR isoform. Immunoprecipitation and measurement of radioactivity can be used to quantify the amount of ligand bound to a CSR in the presence and absence of a CSR isoform. A CSR isoform also can be

assessed for ligand binding such as by incubating a CSR isoform with labeled ligand and determining the amount of labeled ligand bound by a CSR isoform, for example, compared to an amount bound by a wildtype or predominant form of a corresponding CSR.

4. Cell Proliferation assays

A number of RTKs, for example VEGFR, are involved in cell proliferation. Effects of an RTK isoform on cell proliferation can be measured. For example, ligand can be added to cells expressing an RTK. An RTK isoform can be added to such cells before, concurrently or after ligand addition and effects on cell proliferation measured. Alternatively an RTK isoform can be expressed in such cell models, for example using an adenovirus vector. For example, a VEGFR isoform is added to endothelial cells expressing VEGFR. Following isoform addition, VEGF ligand is added and the cells are incubated at standard growth temperature (*e.g.* 37°C) for several days. Cells are trypsinized, stained with trypan blue and viable cells are counted. Cells not exposed to VEGFR isoform and/or ligand are used as controls for comparison. Other suitable controls can be employed.

5. Cell disease model assays

Cells from a disease or condition or that can be modulated to mimic a disease or condition can be used to measure/and or detect the effect of an CSR isoform. Numerous animal and *in vitro* disease models are known to those of skill in the art. For example, a CSR isoform is added or expressed in cells and a phenotype is measured or detected in comparison to cells not exposed to or not expressing a CSR isoform. Such assays can be used to measure effects including effects on cell proliferation, metastasis, inflammation, angiogenesis, pathogen infection and bone resorption.

For example, effects of a MET isoform can be measured using such assays. A liver cell model such as HepG2 liver cells can be used to monitor the infectivity of malaria in culture by sporozoites. An RTK isoform such as a MET isoform can be added to the cells and/or expressed in the cells. Infection of such cells with malaria sporozoites is then measured, such as by staining and counting the EEFs (exoerythrocytic forms) of the sporozoite that are produced as a result of infection

Carrolo *et al.* (2003) *Nat Med 9(11)*:1363-1369. Effects of an RTK isoform can be assessed by comparing results to cells not exposed or expressing an RTK isoform and/or uninfected cells.

Effects of a CSR isoform also can be measured in angiogenesis. For example, tubule formation by endothelial cells such as human umbilical vein endothelial cells (HUVEC) *in vitro* can be used as an assay to measure angiogenesis and effects on angiogenesis. Addition of varying amounts of a CSR isoform to an *in vitro* angiogenesis assay is a method suitable for screening the effectiveness of a CSR isoform as a modulator of angiogenesis.

Bone resorption can be measured in cell culture to measure effectiveness of an RTK-isoform, such as by using osteoclast cultures. Osteoclasts are highly differentiated cells of hematopoietic origin that resorb bone in the organism, and are able to resorb bone from bone slices *in vitro*. Methods for cell culture of osteoclasts and quantitative techniques for measuring bone resorption in osteoclast cell culture have been described in the art. For example, mononuclear cells can be isolated from human peripheral blood and cultured. Addition and/or expression of a CSR isoform can be used to assess effects on osteoclast formation such as by measuring multinucleated cells positive for tartrate-resistant acid phosphatase and resorbed area and collagen fragments released from bone slices. Dose response curves can be used to determine therapeutically effective amounts of a CSR isoform necessary to modulate bone resorption.

6. Animal models

Animal models can be used to assess the effect of a CSR isoform. In one example, animal models of disease can be studied to determine if introduction of a CSR isoform affects the disease. For example, CSR isoform effects on tumor formation including cancer cell proliferation, migration and invasiveness can be measured. In one such assay, cancer cells such as ovarian cancer cells are infected with an adenovirus expressing a CSR isoform. After a culturing period in vitro, cells are trypsinized, suspended in a suitable buffer and injected into mice (e.g., subcutaneously into flanks and shoulders of model mice such as Balb/c nude mice). Tumor growth is monitored over time. Control cells, not expressing a CSR isoform,

can be injected into mice for comparison. Similar assays can be performed with other cell types and animal models, for example, NIH3T3 cells, murine lung carcinoma (LLC) cells, primary Pancreatic Adenocarcinoma (PANC-1) cells, TAKA-1 pancreatic ductal cells, and C57BL/6 mice and SCID mice. In a further example, effects of CSR isoforms on ocular disorders can be assessed using assays such as a corneal micropocket assay. Briefly, mice receive cells expressing a CSR isoform (or control) by injection 2-3 days before the assay. Subsequently, the mice are anesthetized, and pellets of a ligand are implanted into the corneal micropocket of the eyes. Neovascularization is then measured, for example, 5 days following implantation. The effect of a CSR isoform on angiogenesis and eye phenotype compared to a control is then assessed. In an additional example, effects of a CSR isoform in a model of collagen type II-induced arthritis (CIA) can be assessed by intraperitoneal injection of SCID mice with splenocytes from DBA/1 mice that have been transduced with a retroviral vector containing the cDNA of a CSR isoform or unmodified splenocytes. Mice that receive unmodified splenocytes develop arthritis within 11-13 days and can be used as a reference control to determine effects of CSR isoform-expressing splenocytes on the development of arthritis as assessed, for example, by clinical, histological, or immunological (i.e. antibody levels) parameters of arthritis.

Effects of CSR isoforms on animal models of disease additionally can be assessed by the administration of purified or recombinant forms of a CSR isoform. For example, wound healing can be assessed in a model of impaired wound healing utilizing genetically diabetic db+/db+ mice whereby full-thickness excisional wounds are created on the backs of diabetic mice . Following treatment with a CSR isoform, either topically or systemically, wound healing can be assessed by analyzing for wound closure, inflammatory cell infiltration at the site of the wound, and expression of inflammatory cytokines. The effects of CSR isoforms on wound healing can be assessed over time and effects can be compared to mice that receive a control treatment, for example a vehicle only control. In a further example, a recombinant CSR isoform can be administered in a model of pulmonary fibrosis induced by bleomycin or silica to determine if lung fibrosis is reduced as assessed, for example,

by analysis of histological sections for lung damage and by assaying for effects on bleomycin/silica induced increases of lung hydroxyproline content.

Animals deficient in a CSR isoform also can be used to monitor the biological activity of a CSR isoform. For example an isoform-specific disruption can made by creating a targeted construct whereby upstream from an IRES-LacZ cassette, translational stop codons are introduced within the appropriate reading frame to ensure that the receptor protein terminates early. Alternatively, a LoxP/Cre recombination strategy can be used. Following confirmation of the targeted disruption, the consequences of a deficiency in a CSR isoform can be established by analyzing the phenotype of the deficient mice compared to wildtype mice including the development of various organs such as, for example, lung, limbs, eyelids, anterior pituitary gland, and pancreas. In addition, by histology or isolation of specific cell populations, other parameters, such as apoptosis or cell proliferation, can be assessed to determine if there is a difference between animals or isolated cells lacking the CSR isoform compared to wildtype CSR. Components of signaling cascades and expression of downstream genes also can be assessed to determine if the absence of a CSR isoform affects receptor signaling and gene expression.

I. Preparation, Formulation and Administration of CSR isoforms and CSR isoform compositions

CSR isoforms and CSR isoform compositions, including RTK and TNFR isoforms and RTK and TNFR isoform compositions, can be formulated for administration by any route known to those of skill in the art including intramuscular, intravenous, intradermal, intraperitoneal injection, subcutaneous, epidural, nasal oral, rectal, topical, inhalational, buccal (*e.g.*, sublingual), and transdermal administration or any route. CSR isoforms can be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.*, oral mucosa, rectal and intestinal mucosa, etc.) and can be administered with other biologically active agents, either sequentially, intermittently or in the same composition. Administration can be local , topical or systemic depending upon the locus of treatment . Local administration to an area in need of treatment can be achieved by, for example, but not limited to, local infusion during surgery, topical application, *e.g.*, in conjunction with a wound dressing after surgery, by injection, by

means of a catheter, by means of a suppository, or by means of an implant. Administration also can include controlled release systems including controlled release formulations and device controlled release, such as by means of a pump. The most suitable route in any given case will depend on the nature and severity of the disease or condition being treated and on the nature of the particular composition which is used.

Various delivery systems are known and can be used to administer CSR isoforms, such as but not limited to, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor mediated endocytosis, and delivery of nucleic acid molecules encoding CSR isoforms such as retrovirus delivery systems.

Pharmaceutical compositions containing CSR isoforms can be prepared. Generally, pharmaceutically acceptable compositions are prepared in view of approvals for a regulatory agency or other prepared in accordance with generally recognized pharmacopeia for use in animals and in humans. Pharmaceutical compositions can include carriers such as a diluent, adjuvant, excipient, or vehicle with which an isoform is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, and sesame oil. Water is a typical carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions also can be employed as liquid carriers, particularly for injectable solutions. Compositions can contain along with an active ingredient: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethylcellulose; a lubricant, such as magnesium stearate, calcium stearate and talc; and a binder such as starch, natural gums, such as gum acaciagelatin, glucose, molasses, polvinylpyrrolidine, celluloses and derivatives thereof, povidone, crospovidones and other such binders known to those of skill in the art. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, and ethanol. A composition, if desired, also can contain minor amounts of wetting or emulsifying agents, or pH

buffering agents, for example, acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, and sustained release formulations. A composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and other such agents. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. Such compositions will contain a therapeutically effective amount of the compound, generally in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

Formulations are provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. Pharmaceutically therapeutically active compounds and derivatives thereof are typically formulated and administered in unit dosage forms or multiple dosage forms. Each unit dose contains a predetermined quantity of therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical carrier, vehicle or diluent. Examples of unit dose forms include ampoules and syringes and individually packaged tablets or capsules. Unit dose forms can be administered in fractions or multiples thereof. A multiple dose form is a plurality of identical unit dosage forms packaged in a single container to be administered in segregated unit dose form. Examples of multiple dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit doses that are not segregated in packaging.

Dosage forms or compositions containing active ingredient in the range of 0.005% to 100% with the balance made up from non-toxic carrier can be prepared. For oral administration, pharmaceutical compositions can take the form of, for

example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (*e.g.*, pregelatinized maize starch, polyvinyl pyrrolidone 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.

Pharmaceutical preparation also can be in liquid form, for example, solutions, syrups or suspensions, or can be presented as a drug product for reconstitution 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, or fractionated vegetable oils); and preservatives (*e.g.*, methyl or propyl-p-hydroxybenzoates or sorbic acid).

Formulations suitable for rectal administration can be provided as unit dose suppositories. These can be prepared by admixing the active compound with one or more conventional solid carriers, for example, cocoa butter, and then shaping the resulting mixture.

Formulations suitable for topical application to the skin or to the eye include ointments, creams, lotions, pastes, gels, sprays, aerosols and oils. Exemplary carriers include Vaseline, lanoline, polyethylene glycols, alcohols, and combinations of two or more thereof. The topical formulations also can contain 0.05 to 15, 20, 25 percent by weight of thickeners selected from among hydroxypropyl methyl cellulose, methyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, poly (alkylene glycols), poly/hydroxyalkyl, (meth)acrylates or poly(meth)acrylamides. A topical formulation is often applied by instillation or as an ointment into the conjunctival sac. It also can be used for irrigation or lubrication of the eye, facial sinuses, and external auditory meatus. It also can be injected into the anterior eye chamber and other places. A topical formulation in the liquid state can be also present in a hydrophilic three-

dimensional polymer matrix in the form of a strip or contact lens, from which the active components are released.

For administration by inhalation, the compounds for use herein 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 the compound and a suitable powder base such as lactose or starch.

Formulations suitable for buccal (sublingual) administration include, for example, lozenges containing the active compound in a flavored base, usually sucrose and acacia or tragacanth; and pastilles containing the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

Pharmaceutical compositions of CSR isoforms 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 be 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 form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water or other solvents, before use.

Formulations suitable for transdermal administration can be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. Such patches suitably contain the active compound as an optionally buffered aqueous solution of, for example, 0.1 to 0.2M concentration with respect to the active compound. Formulations suitable for transdermal administration also can be delivered by iontophoresis (see, *e.g.*, *Pharmaceutical Research 3(6)*, 318 (1986)) and typically take the form of an optionally buffered aqueous solution of the active compound.

Pharmaceutical compositions also can be administered by controlled release means and/or delivery devices (see, *e.g.*, in U.S. Patent Nos. 3,536,809; 3,598,123; 3,630,200; 3,845,770; 3,847,770; 3,916,899; 4,008,719; 4,687,610; 4,769,027; 5,059,595; 5,073,543; 5,120,548; 5,354,566; 5,591,767; 5,639,476; 5,674,533 and 5,733,566).

In certain embodiments, liposomes and/or nanoparticles may also be employed with CSR isoform administration. Liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs). MLVs generally have diameters of from 25 nm to 4 μm. Sonication of MLVs results in the formation of small unilamellar vesicles (SUVs) with diameters in the range of 200 to 500 .ANG., containing an aqueous solution in the core.

Phospholipids can form a variety of structures other than liposomes when dispersed in water, depending on the molar ratio of lipid to water. At low ratios, the liposomes form. Physical characteristics of liposomes depend on pH, ionic strength and the presence of divalent cations. Liposomes can show low permeability to ionic and polar substances, but at elevated temperatures undergo a phase transition which markedly alters their permeability. The phase transition involves a change from a closely packed, ordered structure, known as the gel state, to a loosely packed, less-ordered structure, known as the fluid state. This occurs at a characteristic phase-transition temperature and results in an increase in permeability to ions, sugars and drugs.

Liposomes interact with cells via different mechanisms: Endocytosis by phagocytic cells of the reticuloendothelial system such as macrophages and neutrophils; adsorption to the cell surface, either by nonspecific weak hydrophobic or electrostatic forces, or by specific interactions with cell-surface components; fusion with the plasma cell membrane by insertion of the lipid bilayer of the liposome into the plasma membrane, with simultaneous release of liposomal contents into the cytoplasm; and by transfer of liposomal lipids to cellular or subcellular membranes, or vice versa, without any association of the liposome contents. Varying the liposome formulation can alter which mechanism is operative, although more than one may

operate at the same time. Nanocapsules can generally entrap compounds in a stable and reproducible way. To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) should be designed using polymers able to be degraded in vivo. Biodegradable polyalkyl-cyanoacrylate nanoparticles that meet these requirements are contemplated for use herein, and such particles can be easily made.

Administration methods can be employed to decrease the exposure of CSR isoforms to degradative processes, such as proteolytic degradation and immunological intervention via antigenic and immunogenic responses. Examples of such methods include local administration at the site of treatment. Pegylation of therapeutics has been reported to increase resistance to proteolysis; increase plasma half-life, and decrease antigenicity and immunogenicity. Examples of pegylation methodologies are known in the art (see for example, Lu and Felix, *Int. J. Peptide Protein Res., 43*: 127-138, 1994; Lu and Felix, *Peptide Res., 6:* 142-6, 1993; Felix *et al.*, *Int. J. Peptide Res., 46* : 253-64, 1995; Benhar *et al.*, *J. Biol. Chem., 269*: 13398-404, 1994; Brumeanu *et al.*, *J Immunol., 154*: 3088-95, 1995; see also, Caliceti *et al.* (2003) *Adv. Drug Deliv. Rev. 55(10)*:1261-77 and Molineux (2003) *Pharmacotherapy 23 (8 Pt 2)*:3S-8S). Pegylation also can be used in the delivery of nucleic acid molecules in vivo. For example, pegylation of adenovirus can increase stability and gene transfer (see, e.g., Cheng *et al.* (2003) *Pharm. Res. 20(9)*: 1444-51).

Desirable blood levels can be maintained by a continuous infusion of the active agent as ascertained by plasma levels. It should be noted that the attending physician would know how to and when to terminate, interrupt or adjust therapy to lower dosage due to toxicity, or bone marrow, liver or kidney dysfunctions. Conversely, the attending physician would also know how to and when to adjust treatment to higher levels if the clinical response is not adequate (precluding toxic side effects). administered, for example, by oral, pulmonary, parental (intramuscular, intraperitoneal, intravenous (IV) or subcutaneous injection), inhalation (via a fine powder formulation), transdermal, nasal, vaginal, rectal, or sublingual routes of administration and can be formulated in dosage forms appropriate for each route of

administration (see, *e.g.*, International PCT application Nos. WO 93/25221 and WO 94/17784; and European Patent Application 613,683).

A CSR isoform 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 patient treated. 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 concentration a CSR isoform in the composition will depend on absorption, inactivation and excretion rates of the complex, the physicochemical characteristics of the complex, the dosage schedule, and amount administered as well as other factors known to those of skill in the art. The amount of a CSR isoform to be administered for the treatment of a disease or condition, for example cancer, autoimmune disease and infection can be determined by standard clinical techniques. In addition, *in vitro* assays and animal models can be employed to help identify optimal dosage ranges. The precise dosage, which can be determined empirically, can depend on the route of administration and the seriousness of the disease. Suitable dosage ranges for administration can range from about 0.01 pg/kg body weight to 1 mg/kg body weight and more typically 0.05 mg/kg to 200 mg/kg CSR isoform: patient weight.

A CSR isoform can be administered at once, or can be divided into a number of smaller doses to be administered at intervals of time. CSR isoforms can be administered in one or more doses over the course of a treatment time for example over several hours, days, weeks, or months. In some cases, continuous administration is useful. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and can be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values also can vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein

are exemplary only and are not intended to limit the scope or use of compositions and combinations containing them.

J. *In Vivo* Expression of CSR isoforms and Gene therapy

CSR isoforms can be delivered to cells and tissues by expression of nucleic acid molecules. CSR isoforms can be administered as nucleic acid molecules encoding a CSR isoform, including *ex vivo* techniques and direct *in vivo* expression.

1. Delivery of nucleic acids

Nucleic acids can be delivered to cells and tissues by any method known to those of skill in the art.

a. Vectors – episomal and integrating

Methods for administering CSR isoforms 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.

CSR isoforms also can be used in *ex vivo* gene expression therapy using non-viral vectors. For example, cells can be engineered to express a CSR isoform, such as by integrating a CSR isoform 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.

Viral vectors, include, for example adenoviruses, herpes viruses, retroviruses and others designed for gene therapy can be employed. The vectors can remain episomal or can integrate into chromosomes of the treated subject. A CSR isoform 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 CSR isoform-expressing adenovirus vector. After a suitable

culturing period, the transduced cells are administered to a subject, locally and/or systemically. Alternatively, CSR isoform-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. 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. 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.

A CSR isoform can be expressed by a virus and the virus administered to a subject in need of treatment. Virus vectors suitable for gene therapy include, for example, adenovirus, adeno-associated virus, retroviruses, lentiviruses 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 CSR isoform-expressing adenovirus vector. After a suitable culturing period, the transduced cells are administered to a subject, locally and/or systemically. As another example, CSR isoform-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. 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. 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. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may 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.

b. Artificial chromosomes and other non-viral vector delivery methods

CSR isoforms also can be used in *ex vivo* gene expression therapy using non-viral vectors. For example, cells can be engineered which express a CSR isoform, such as by integrating a CSR isoform sequence 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.

The nucleic acid molecules can be introduced into artificial chromosomes and other non-viral vectors. Artificial chromosomes (see, *e.g.*, U.S. Patent No. 6,077,697 and PCT International PCT application No. WO 02/097059) can be engineered to encode and express the isoform.

c. Liposomes and other encapsulated forms and administration of cells containing the nucleic acids

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.

2. *In vitro* and *Ex vivo* delivery

For *ex vivo* and *in vivo* methods, nucleic acid molecules encoding the CSR isoform is introduced into cells that are from a suitable donor or the subject to be treated. *In vivo* expression of a CSR isoform can be linked to expression of additional molecules. For example, expression of a CSR isoform 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 a CSR isoform can be used to enhance the cytotoxicity of the virus.

In vivo expression of a CSR isoform can include operatively linking a CSR isoform encoding nucleic acid molecule to specific regulatory sequences such as a cell-specific or tissue-specific promoter. CSR isoforms 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 CSR isoform expression.

Cells into which a nucleic acid can be introduced for purposes of therapy encompass 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. Tumor cells also can be target cells for in vivo expression of CSR isoforms. Cells used for in vivo expression of an isoform also include cells autologous to the patient. Such cells can be removed from a patient, nucleic acids for expression of a CSR isoform introduced, and then administered to a patient such as by injection or engraftment.

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 CSR isoforms 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.

For *ex vivo* treatment, cells from a donor compatible with the subject to be treated or the subject to be treated cells 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 CSR isoforms *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 CSR isoform can be linked to expression of additional molecules. For example, expression of a CSR isoform 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 CSR isoform can be used to enhance the cytotoxicity of the virus.

In vivo expression of a CSR isoform can include operatively linking a CSR isoform encoding nucleic acid molecule to specific regulatory sequences such as a cell-specific or tissue-specific promoter. CSR isoforms also can be expressed from vectors that specifically infect and/or replicate in target cell types and/or tissues. Inducible promoters can selectively regulate CSR isoform expression.

3. Systemic, local and topical delivery

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 cell that typically targets a cell or tissue. For example, tumor cells and proliferating cells can be targeted cells for *in vivo* expression of CSR isoforms. Cells used for *in vivo*

expression of an isoform also include cells autologous to the patient. Such cells can be removed from a patient, nucleic acids for expression of a CSR isoform introduced, and then administered to a patient such as by injection or engraftment.

K. CSRs and Angiogenesis

CSRs participate in pathways involved in a variety of pathways, including those that participate in angiogenesis, cell proliferation, inflammatory responses, and neovascularization among others. Angiogenesis is a process by which new blood vessels are formed. It occurs in healthy individuals, such as during wound healing and in aberrant conditions, such as in tumors.. It occurs for example, in a healthy body in would healing and for restoring blood flow to tissues after injury or insult. Angiogenesis is a component of tumorigenesis, which requires the growth of blood cells to feed the growing tumorous mass. In females, angiogenesis also occurs during the monthly reproductive cycle to rebuild the uterus lining, to mature the egg during ovulation and during pregnancy to build the placenta.

Angiogenesis is controlled through a series of "on" and "off" switches. The primary "on" switches are angiogenesis-stimulating growth factors. The primary "off switches" are angiogenesis inhibitors. When angiogenic growth factors are produced in excess of angiogenesis inhibitors, the balance can be in favor of blood vessel growth. When inhibitors are present in excess of stimulators, angiogenesis is stopped. A healthy body maintains a balance of angiogenesis modulators. A number of angiogenic growth factors are known. These include, for example, angiogenin, angiopoietin-1, Del-1, fibroblast growth factors: acidic (aFGF) and basic (bFGF), follistatin, granulocyte colony-stimulating factor (G-CSF), hepatocyte growth factor (HGF), scatter factor (SF), interleukin-8 (IL-8), leptin, midkine, placental growth factor, platelet-derived endothelial cell growth factor (PD-ECGF), platelet-derived growth factor-BB (PDGF-BB), pleiotrophin (PTN), progranulin, proliferin, transforming growth factor-alpha (TGF-alpha), transforming growth factor-beta (TGF-beta), tumor necrosis factor-alpha (TNF-alpha), and vascular endothelial growth factor (VEGF)/vascular permeability factor (VPF).

1. Angiogenesis and disease

Cellular receptors for angiogenic factors (positive and negative) can act as points of intervention in multiple disease processes, for example, in diseases and conditions where the balance of angiogenic growth factors has been altered and/or the amount or timing of angiogenesis is altered.. For example, in some situations 'too much' angiogenesis can be detrimental, such as angiogenesis that supplies blood to tumor foci, in inflammatory responses and other aberrant angiogenic-related conditions. The growth of tumors, or sites of proliferation in chronic inflammation, generally requires the recruitment of neighboring blood vessels and vascular endothelial cells to support their metabolic requirements. This is because the diffusion is limited for oxygen in tissues. Exemplary conditions that require angiogenesis include, but are not limited to solid tumors and hematologic malignancies such as lymphomas, acute leukemia, and multiple myeloma, where increased numbers of blood vessels are observed in the pathologic bone marrow.

A critical element in the growth of primary tumors and formation of metastatic sites is the angiogenic switch: the ability of the tumor or inflammatory site to promote the formation of new capillaries from preexisting host vessels. The angiogenic switch, as used in this context, refers to disease-associated angiogenesis required for the progression of cancer and inflammatory diseases, such as rheumatoid arthritis. It is a switch that activates a cascade of physiological activities that finally result in the extension of new blood vessels to support the growth of diseased tissue. Stimuli for neo-angiogenesis include hypoxia, inflammation, and genetic lesions in oncogenes or tumor suppressors that alter disease cell gene expression.

Angiogenesis also play a role in inflammatory diseases. These diseases have a proliferative component, similar to a tumor focus. In rheumatoid arthritis, one component of this is characterized by aberrant proliferation of synovial fibroblasts, resulting in pannus formation. The pannus is composed of synovial fibroblasts which have some phenotypic characteristics with transformed cells. As a pannus grows within the joint it expresses many proangiogenic signals, and experiences many of the same neo-angiogenic requirements as a tumor. The need for additional blood supply, neoangiogenesis, is critical. Similarly, many chronic inflammatory conditions also

have a proliferative component in which some of the cells composing it may have characteristics usually attributed to transformed cells.

Another example of a condition involving excess angiogenesis is diabetic retinopathy (Lip et al. Br J Ophthalmology 88: 1543, 2004)). Diabetic retinopathy has angiogenic, inflammatory and proliferative components; overexpression of VEGF, and angiopoietin-2 are common. This overexpression is likely required for disease-associated remodeling and branching of blood vessels, which then supports the proliferative component of the disease.

2. Angiogenesis

Angiogenesis includes several steps, including the recruitment of circulating endothelial cell precursors (CEPs), stimulation of new endothelial cell (EC) growth by growth factors, the degradation of the ECM by proteases, proliferation of ECs and migration into the target, which could be a tumor site or another proliferative site caused by inflammation. This results in the eventual formation of new capillary tubes. Such blood vessels are not necessarily normal in structure. They may have chaotic architecture and blood flow. Due to an imbalance of angiogenic regulators such as vascular endothelial growth factor, (VEGF) and angiopoietins, the new vessels supplying tumorous or inflammatory sites are tortuous and dilated with an uneven diameter, excessive branching, and shunting. Blood flow is variable, with areas of hypoxia and acidosis leading to the selection of variants that are resistant to hypoxia-induced apoptosis (often due to the loss of p53 expression); and enhanced production of proangiogenic signals. Disease-associated vessel walls have numerous openings, widened interendothelial junctions, and discontinuous or absent basement membrane; this contributes to the high vascular permeability of these vessels and, together with lack of functional lymphatics/drainage, causes interstitial hypertension. Disease-associated blood vessels may lack perivascular cells such as pericytes and smooth muscle cells that normally regulate vasoactive control in response to tissue metabolic needs. Unlike normal blood vessels, the vascular lining of tumor vessels is not a homogenous layer of ECs but often consists of a mosaic of ECs and tumor cells; the concept of cancer cell–derived vascular channels, which may be lined by ECM secreted by the tumor cells, is referred to as vascular mimicry.

A similar situation occurs where blood vessels rapidly invade sites of acute inflammation. The ECs of angiogenic blood vessels are unlike quiescent ECs found in adult vessels, where only 0.01% of ECs are dividing. During tumor angiogenesis, ECs are highly proliferative and express a number of plasma membrane proteins that are characteristic of activated endothelium, including growth factor receptors and adhesion molecules such as integrins. Tumors utilize a number of mechanisms to promote their vascularization, and in each case they subvert normal angiogenic processes to suit this purpose. For this reason, increased production of angiogenic factors, both proliferative with respect to endothelium; and structural (allowing for increased branching of the neovasculature) are likely to occur in disease foci, as in cancer or chronic inflammatory disease.

3. Cell surface receptors in Angiogenesis

Cell surface receptors including RTKs, and their ligands play a role in the regulation of angiogenesis (see for example, Figure 1). Angiogenic endothelium expresses a number of receptors not found on resting endothelium. These include receptor tyrosine kinases (RTK) and integrins that bind to the extracellular matrix and mediate endothelial cells adhesion, migration, and invasion.

Endothelial cells (ECs) also express RTK (*i.e.*, the FGF and PDGF receptors) that are found on many other cell types. Functions mediated by activated RTK include proliferation, migration, and enhanced survival of endothelial cells, as well as regulation of the recruitment of perivascular cells and bloodborne circulating endothelial precursors and hematopoietic stem cells to the tumor. One example of a CSR involved in angiogenesis is VEGFR. VEGFR-1 receptors and VEGF-A ligand are involved in cell proliferation, migration and differentiation in angiogenesis. VEGF-A is a heparin-binding glycoprotein with at least four isoforms that regulate blood vessel formation by binding to RTKs, VEGFR-1 and VEGFR-2. These VEGF receptors are expressed on all ECs in addition to a subset of hematopoietic cells. VEGFR-2 regulates EC proliferation, migration, and survival, while VEGFR-1 may act as an antagonist of R1 in ECs but also can plays a role in angioblast differentiation during embryogenesis.

Additional signaling pathways also are involved in angiogenesis. The angiopoietin, Ang1, produced by stromal cells, binds to the EC RTK TEK and promotes the interaction of ECs with the ECM and perivascular cells, such as pericytes and smooth muscle cells, to form tight, non-leaky vessels. PDGF and basic fibroblast growth factor (bFGF) help to recruit these perivascular cells. Ang1 is required for maintaining the quiescence and stability of mature blood vessels and prevents the vascular permeability normally induced by VEGF and inflammatory cytokines.

Proangiogenic cytokines, chemokines, and growth factors secreted by stromal cells or inflammatory cells make important contributions to neovascularization, including bFGF, transforming growth factor-alpha, TNF-alpha, and IL-8. In contrast to normal endothelium, angiogenic endothelium overexpresses specific members of the integrin family of ECM-binding proteins that mediate EC adhesion, migration, and survival. Integrins mediate spreading and migration of ECs and are required for angiogenesis induced by VEGF and bFGF, which in turn can upregulate EC integrin expression. EC adhesion molecules can be upregulated (i.e., by VEGF, TNF-alpha). VEGF promotes the mobilization and recruitment of circulating endothelial cell precursors (CEPs) and hematopoietic stem cells (HSCs) to tumors where they colocalize and appear to cooperate in neovessel formation. CEPs express VEGFR-2, while HSCs express VEGFR-1, a receptor, or VEGF and PlGF. Both CEPs and HSCs are derived from a common precursor, the hemangioblast. CEPs are thought to differentiate into ECs, whereas the role of HSC-derived cells (such as tumor-associated macrophages) may be to secrete angiogenic factors required for sprouting and stabilization of ECs (VEGF, bFGF, angiopoietins) and to activate MMPs, resulting in ECM remodeling and growth factor release. In mouse tumor models and in human cancers, increased numbers of CEPs and subsets of VEGFR-1 or VEGFR-expressing HSCs can be detected in the circulation, which may correlate with increased levels of serum VEGF.

4. Tumor and inflammatory diseases

Tumors secrete trophic angiogenic molecules, such as VEGF family of endothelial growth factors, that induce the proliferation and migration of host ECs

into the tumor. Tumor vessels appear to be more dependent on VEGFR signaling for growth and survival than normal ECs. Sprouting in normal and pathogenic angiogenesis is regulated by three families of transmembrane RTKs expressed on ECs and their ligand: VEGFs, angiopoietins, and ephrins, which are produced by tumor cells, inflammatory cells, or stromal cells in the microenvironment of the disease site. Tumor or inflammatory disease-associated angiogenesis is a complex process involving many different cell types that proliferate, migrate, invade, and differentiate in response to signals from microenvironment. Endothelial cells (ECs) sprout from host vessels in response to VEGF, bFGF, Ang2, and other proangiogenic stimuli. Sprouting is stimulated by VEGF/VEGFR-2, Ang2/TEK, and integrin/extracellular matrix (ECM) interactions. Bone marrow–derived circulating endothelial precursors (CEPs) migrate to the tumor in response to VEGF and differentiate into ECs, while hematopoietic stem cells differentiate into leukocytes, including tumor/disease site-associated macrophages that secrete angiogenic growth factors and produce MMPs that remodel the ECM and release bound growth factors.

When tumor cells arise in or metastasize to an avascular area, they grow to a size limited by hypoxia and nutrient deprivation. This condition, also likely to occur in other localized proliferative diseases, leads to the selection of cells that produce angiogenic factors. Hypoxia, a key regulator of tumor angiogenesis, causes the transcriptional induction of the gene(s) encoding VEGF by a process that involves stabilization of the transcription factor hypoxia-inducible factor (HIF)1. Under normoxic conditions, EC HIF-1 levels are maintained at a low level by proteasome-mediated destruction regulated by a ubiquitin E3-ligase encoded by the VHL (Von Hippel-Lindau) tumor-suppressor locus. However, under hypoxic conditions, the HIF-1 protein is not hydroxylated and association with VHL does not occur; therefore HIF-1 levels increase, and target genes including VEGF, nitric oxide synthetase (NOS), and Ang2 are induced. Loss of the VHL genes, as occurs in familial and sporadic renal cell carcinomas, also results in HIF-1 stabilization and induction of VEGF. Most tumors have hypoxic regions due to poor blood flow, and tumor cells in these areas stain positive for HIF-1 expression. These are conditions that lead to the de novo formation of blood vessels from differentiating endothelial

cells, as occurs during embryonic development, and angiogenesis under normal (wound healing, corpus luteum formation) and pathologic processes (tumor angiogenesis, inflammatory conditions such as rheumatoid arthritis).

For diseased cell–derived VEGF, such as may be produced by a growing tumor focus or by pannus formation in rheumatoid arthritis, to initiate sprouting from host vessels, the stability conferred by the Ang1/TEK pathway must be perturbed; this occurs by the secretion of Ang2 by ECs that are undergoing active remodeling. Ang2 binds to TEK and is a competitive inhibitor of Ang1 action: under the influence of Ang2, preexisting blood vessels become more responsive to remodeling signals, with less adherence of ECs to stroma and associated perivascular cells and more responsiveness to VEGF. Therefore, Ang2 is required at early stages of neoangiogenesis for destabilizing the vasculature by making host ECs more sensitive to angiogenic signals. Since tumor ECs are blocked by Ang2, there is no stabilization by the Ang1/TEK interaction, and tumor blood vessels are leaky, hemorrhagic, and have poor association of ECs with underlying stroma. Sprouting tumor ECs express high levels of the transmembrane protein Ephrin-B2 and its receptor, the RTK EPH whose signaling appears to work with the angiopoietins during vessel remodeling. During embryogenesis, EPH receptors are expressed on the endothelium of primordial venous vessels while the transmembrane ligand ephrin-B2 is expressed by cells of primordial arteries; the reciprocal expression may regulate differentiation and patterning of the vasculature.

Development of tumor lymphatics also is associated with expression of cell surface receptors, including VEGFR-3 and its ligands VEGF-C and VEGF-D. The role of these vessels in tumor cell metastasis to regional lymph nodes remains to be determined, since, as discussed above, interstitial pressures within tumors are high and most lymphatic vessels may exist in a collapsed and nonfunctional state. However, VEGF-C levels in primary human tumors, including lung, prostate, and colorectal cancers, correlate significantly with metastasis to regional lymph nodes, and therefore it is possible that expression of VEGF-C,D/R3 may contribute to disease spreading by maintaining an exit for tumor cells from the primary site to lymph nodes and beyond.

5. Cell surface receptors and treatment of angiogenic diseases and conditions

Modulation of angiogenesis, neovascularization and/or cell proliferation can be used to treat diseases and conditions in which angiogenesis plays a role. For example, angiogenesis inhibitors can function by targeting the critical molecular pathways involved in EC proliferation, migration, and/or survival, many of which are unique to the activated endothelium in tumors. Inhibition of growth factor and adhesion-dependent signaling pathways can induce EC apoptosis with concomitant inhibition of tumor growth. ECs comprising the tumor vasculature are genetically stable and do not share genetic changes with tumor cells; the EC apoptosis pathways are therefore intact. Each EC of a tumor vessel helps provide nourishment to many tumor cells, and although tumor angiogenesis can be driven by a number of exogenous proangiogenic stimuli, experimental data indicate that blockade of a single growth factor (*e.g.*, VEGF) can inhibit tumor-induced vascular growth. Because tumor blood vessels are distinct from normal ones, they may be selectively destroyed without affecting normal vessels.

Because cell surface receptors are involved in the regulation of angiogenesis, they can be therapeutic targets for treatment of diseases and conditions involving angiogenesis. Provided herein are CSR isoforms that can modulate one or more steps in the angiogenic process. CSR isoforms can be administered singly, in parallel or in other combinations. For instance, angiogenesis induced by bFGF can be blocked by inhibitors of the bFGFR such as a CSR isoform, and this can in turn inhibit activation of the VEGF pathway. The VEGFR pathway also can be blocked by a VEGFR isoform. CSR isoforms that modulate Ang/TEK and Ephrin/EPH pathways also can be administered to modulate angiogenesis. CSR isoforms that act as antagonists of the activity of VEGFR, bFGF, Ang2, TNF-alpha, TGF-alpha, and other factors such as ephrin antagonists, can be administered. These ligands and their receptors are required for the attraction of new endothelial cells, and/or their structural transformation into blood vessels by differentiation from circulating endothelial precursors (CEPs) or by inhibiting either tube formation or the needed branching. Hence, antagonizing one or more of these factors can inhibit the development and

progression of cancer and inflammatory disease. As described herein, CSR isoforms can be administered as therapeutics for such diseases and conditions.

L. Exemplary Treatments and Studies with CSR isoforms

Provided herein are methods of treatment with CSR isoforms for diseases and conditions. CSR isoforms such as RTK isoforms and TNFR isoforms can be used in the treatment of a variety of diseases and conditions, including those described herein. Treatment can be effected by administering by suitable route formulations of the polypeptides, which can be provided in compositions as polypeptides and can be linked to targeting agents, for targeted delivery or encapsulated in delivery vehicles, such as liposomes. Alternatively, nucleic acids encoding the polypeptides can be administered as naked nucleic acids or in vectors, particularly gene therapy vectors. Gene therapy can be effected by any method known to those of skill in the art. Gene therapy can be effected *in vivo* by directly administering the nucleic acid or vector. For example, the nucleic acids can be delivered systemically, locally, topically or by any suitable route. The vectors or nucleic acids can be targeted by including targeting agents in delivery vehicle, such as a virus or liposome, or they can be conjugated to a targeting agent, such as an antibody. The vectors or nucleic acids can be introduced into cells *ex vivo* by removing cells from a subject or suitable donor, introducing the vector or nucleic acid into the cells and then introducing the modified cells into the subject.

The CSR isoforms provided herein can be used for treating a variety of disorders, particularly proliferative, immune and inflammatory disorders. Treatments, include, but are not limited to treatment of angiogenesis-related diseases and conditions including ocular diseases, atherosclerosis, cancer and vascular injuries, neurodegenerative diseases, including Alzheimer's disease, inflammatory diseases and conditions, including atherosclerosis, diseases and conditions associated with cell proliferation including cancers, and smooth muscle cell-associated conditions, and various autoimmune diseases. Exemplary treatments and preclinical studies are described for treatments and therapies with RTK and TNFR isoforms. Such descriptions are meant to be exemplary only and are not limited to a particular RTK or TNFR isoform. The particular treatment and dosage can be determined by one of

skill in the art. Considerations in assessing treatment include, the disease to be treated, the severity and course of the disease, whether the molecule is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to therapy, and the discretion of the attending physician.

1. Angiogenesis-related conditions

RTK isoforms including, but not limited to, VEGFR, PDGFR, TIE/TEK, EGFR, and EphA and TNFR isoforms including TNFR1 and TNFR2 can be used in treatment of angiogenesis- related diseases and conditions, such as ocular diseases and conditions, including ocular diseases involving neovascularization. Ocular neovascular disease is characterized by invasion of new blood vessels into the structures of the eye, such as the retina or cornea. It is the most common cause of blindness and is involved in approximately twenty eye diseases. In age-related macular degeneration, the associated visual problems are caused by an ingrowth of choroidal capillaries through defects in Bruch's membrane with proliferation of fibrovascular tissue beneath the retinal pigment epithelium. Angiogenic damage also is associated with diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma and retrolental fibroplasia. Other diseases associated with corneal neovascularization include, but are not limited to, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogrens, acne rosacea, phylectenulosis, syphilis, Mycobacteria infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, Herpes simplex infections, Herpes zoster infections, protozoan infections, Karposi sarcoma, Mooren ulcer, Terrien's marginal degeneration, marginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegeners sarcoidosis, Scleritis, Steven's Johnson disease, periphigoid radial keratotomy, and corneal graph rejection. Diseases associated with retinal/choroidal neovascularization include, but are not limited to, diabetic retinopathy, macular degeneration, sickle cell anemia, sarcoid, syphilis, pseudoxanthoma elasticum, Pagets disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis/vitritis, mycobacterial infections, Lyme's disease, systemic lupus erythematosus, retinopathy of prematurity, Eales disease, Bechets disease, infections

causing a retinitis or choroiditis, presumed ocular histoplasmosis, Bests disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, trauma and post-laser complications. Other diseases include, but are not limited to, diseases associated with rubeosis (neovascularization of the angle) and diseases caused by the abnormal proliferation of fibrovascular or fibrous tissue including all forms of proliferative vitreoretinopathy.

RTK and TNFR isoform therapeutic effects on angiogenesis such as in treatment of ocular diseases can be assessed in animal models, for example in cornea implants, such as described herein. For example, modulation of angiogenesis such as for an RTK can be assessed in a nude mouse model such as epidermoid A431 tumors in nude mice and VEGF-or PIGF-transduced rat C6 gliomas implanted in nude mice. CSR isoforms can be injected as protein locally or systemically. Alternatively cells expressing CSR isoforms can be inoculated locally or at a site remote to the tumor. Tumors can be compared between control treated and CSR isoform treated models to observe phenotypes of tumor inhibition including poorly vascularized and pale tumors, necrosis, reduced proliferation and increased tumor-cell apoptosis. In one such treatment, Flt-1 isoforms are used to treat ocular disease and assessed in such models.

Examples of ocular disorders that can be treated with TIE/TEK isoforms are eye diseases characterized by ocular neovascularization including, but not limited to, diabetic retinopathy (a major complication of diabetes), retinopathy of prematurity (this devastating eye condition, that frequently leads to chronic vision problems and carries a high risk of blindness, is a severe complication during the care of premature infants), neovascular glaucoma, retinoblastoma, retrolental fibroplasia, rubeosis, uveitis, macular degeneration, and corneal graft neovascularization. Other eye inflammatory diseases, ocular tumors, and diseases associated with choroidal or iris neovascularization also can be treated with TIE/TEK isoforms.

PDGFR isoforms also can be used in the treatment of proliferative vitreoretinopathy. For example, an expression vector such as a retroviral vector is constructed containing a nucleic acid molecule encoding a PDGFR isoform. Rabbit conjunctival fibroblasts (RCFs) are produced which contain the expression vector by

Additional signaling pathways also are involved in angiogenesis. The angiopoietin, Ang1, produced by stromal cells, binds to the EC RTK Tie-2 and promotes the interaction of ECs with the ECM and perivascular cells, such as pericytes and smooth muscle cells, to form tight, non-leaky vessels. PDGF and basic fibroblast growth factor (bFGF) help to recruit these perivascular cells. Ang1 is required for maintaining the quiescence and stability of mature blood vessels and prevents the vascular permeability normally induced by VEGF and inflammatory cytokines.

Proangiogenic cytokines, chemokines, and growth factors secreted by stromal cells or inflammatory cells make important contributions to neovascularization, including bFGF, transforming growth factor-alpha, TNF-alpha, and IL-8. In contrast to normal endothelium, angiogenic endothelium overexpresses specific members of the integrin family of ECM-binding proteins that mediate EC adhesion, migration, and survival. Integrins mediate spreading and migration of ECs and are required for angiogenesis induced by VEGF and bFGF, which in turn can upregulate EC integrin expression. EC adhesion molecules can be upregulated (i.e., by VEGF, TNF-alpha). VEGF promotes the mobilization and recruitment of circulating endothelial cell precursors (CEPs) and hematopoietic stem cells (HSCs) to tumors where they colocalize and appear to cooperate in neovessel formation. CEPs express VEGFR2, while HSCs express VEGFR1, a receptor, or VEGF and PlGF. Both CEPs and HSCs are derived from a common precursor, the hemangioblast. CEPs are thought to differentiate into ECs, whereas the role of HSC-derived cells (such as tumor-associated macrophages) may be to secrete angiogenic factors required for sprouting and stabilization of ECs (VEGF, bFGF, angiopoietins) and to activate MMPs, resulting in ECM remodeling and growth factor release. In mouse tumor models and in human cancers, increased numbers of CEPs and subsets of VEGFR1 or VEGFR-expressing HSCs can be detected in the circulation, which may correlate with increased levels of serum VEGF.

4. Tumor and inflammatory diseases

Tumors secrete trophic angiogenic molecules, such as VEGF family of endothelial growth factors, that induce the proliferation and migration of host ECs

into the tumor. Tumor vessels appear to be more dependent on VEGFR signaling for growth and survival than normal ECs. Sprouting in normal and pathogenic angiogenesis is regulated by three families of transmembrane RTKs expressed on ECs and their ligand: VEGFs, angiopoietins, and ephrins, which are produced by tumor cells, inflammatory cells, or stromal cells in the microenvironment of the disease site. Tumor or inflammatory disease-associated angiogenesis is a complex process involving many different cell types that proliferate, migrate, invade, and differentiate in response to signals from microenvironment. Endothelial cells (ECs) sprout from host vessels in response to VEGF, bFGF, Ang2, and other proangiogenic stimuli. Sprouting is stimulated by VEGF/VEGFR2, Ang2/Tie-2, and integrin/extracellular matrix (ECM) interactions. Bone marrow–derived circulating endothelial precursors (CEPs) migrate to the tumor in response to VEGF and differentiate into ECs, while hematopoietic stem cells differentiate into leukocytes, including tumor/disease site-associated macrophages that secrete angiogenic growth factors and produce MMPs that remodel the ECM and release bound growth factors.

When tumor cells arise in or metastasize to an avascular area, they grow to a size limited by hypoxia and nutrient deprivation. This condition, also likely to occur in other localized proliferative diseases, leads to the selection of cells that produce angiogenic factors. Hypoxia, a key regulator of tumor angiogenesis, causes the transcriptional induction of the gene(s) encoding VEGF by a process that involves stabilization of the transcription factor hypoxia-inducible factor (HIF)1. Under normoxic conditions, EC HIF-1 levels are maintained at a low level by proteasome-mediated destruction regulated by a ubiquitin E3-ligase encoded by the VHL (Von Hippel-Lindau) tumor-suppressor locus. However, under hypoxic conditions, the HIF-1 protein is not hydroxylated and association with VHL does not occur; therefore HIF-1 levels increase, and target genes including VEGF, nitric oxide synthetase (NOS), and Ang2 are induced. Loss of the VHL genes, as occurs in familial and sporadic renal cell carcinomas, also results in HIF-1 stabilization and induction of VEGF. Most tumors have hypoxic regions due to poor blood flow, and tumor cells in these areas stain positive for HIF-1 expression. These are conditions that lead to the de novo formation of blood vessels from differentiating endothelial

cells, as occurs during embryonic development) and angiogenesis under normal (wound healing, corpus luteum formation) and pathologic processes (tumor angiogenesis, inflammatory conditions such as rheumatoid arthritis).

For diseased cell–derived VEGF, such as may be produced by a growing tumor focus or by pannus formation in rheumatoid arthritis, to initiate sprouting from host vessels, the stability conferred by the Ang1/Tie2 pathway must be perturbed; this occurs by the secretion of Ang2 by ECs that are undergoing active remodeling. Ang2 binds to Tie2 and is a competitive inhibitor of Ang1 action: under the influence of Ang2, preexisting blood vessels become more responsive to remodeling signals, with less adherence of ECs to stroma and associated perivascular cells and more responsiveness to VEGF. Therefore, Ang2 is required at early stages of neoangiogenesis for destabilizing the vasculature by making host ECs more sensitive to angiogenic signals. Since tumor ECs are blocked by Ang2, there is no stabilization by the Ang1/Tie2 interaction, and tumor blood vessels are leaky, hemorrhagic, and have poor association of ECs with underlying stroma. Sprouting tumor ECs express high levels of the transmembrane protein Ephrin-B2 and its receptor, the RTK EPH whose signaling appears to work with the angiopoietins during vessel remodeling. During embryogenesis, EPH receptors are expressed on the endothelium of primordial venous vessels while the transmembrane ligand ephrin-B2 is expressed by cells of primordial arteries; the reciprocal expression may regulate differentiation and patterning of the vasculature.

Development of tumor lymphatics also is associated with expression of cell surface receptors, including VEGFR3 and its ligands VEGF-C and VEGF-D. The role of these vessels in tumor cell metastasis to regional lymph nodes remains to be determined, since, as discussed above, interstitial pressures within tumors are high and most lymphatic vessels may exit in a collapsed and nonfunctional state. However, VEGF-C levels in primary human tumors, including lung, prostate, and colorectal cancers, correlate significantly with metastasis to regional lymph nodes, and therefore it is possible that expression of VEGF-C,D/R3 may contribute to disease spreading by maintaining an exit for tumor cells from the primary site to lymph nodes and beyond.

5. Cell surface receptors and treatment of angiogenic diseases and conditions

Modulation of angiogenesis, neovascularization and/or cell proliferation can be used to treat diseases and conditions in which angiogenesis plays a role. For example, angiogenesis inhibitors can function by targeting the critical molecular pathways involved in EC proliferation, migration, and/or survival, many of which are unique to the activated endothelium in tumors. Inhibition of growth factor and adhesion-dependent signaling pathways can induce EC apoptosis with concomitant inhibition of tumor growth. ECs comprising the tumor vasculature are genetically stable and do not share genetic changes with tumor cells; the EC apoptosis pathways are therefore intact. Each EC of a tumor vessel helps provide nourishment to many tumor cells, and although tumor angiogenesis can be driven by a number of exogenous proangiogenic stimuli, experimental data indicate that blockade of a single growth factor (e.g., VEGF) can inhibit tumor-induced vascular growth. Because tumor blood vessels are distinct from normal ones, they may be selectively destroyed without affecting normal vessels.

Because cell surface receptors are involved in the regulation of angiogenesis, they can be therapeutic targets for treatment of diseases and conditions involving angiogenesis. Provided herein are CSR isoforms that can modulate one or more steps in the angiogenic process. CSR isoforms can be administered singly, in parallel or in other combinations. For instance, angiogenesis induced by bFGF can be blocked by inhibitors of the bFGFR such as a CSR isoform, and this can in turn inhibit activation of the VEGF pathway. The VEGFR pathway also can be blocked by a VEGFR isoform. CSR isoforms that modulate Ang/Tie2 and Ephrin/EPH pathways also can be administered to modulate angiogenesis. CSR isoforms that act as antagonists of the activity of VEGFR, bFGF, Ang2, TNF-alpha, TGF-alpha, and other factors such as ephrin antagonists, can be administered. These ligands and their receptors are required for the attraction of new endothelial cells, and/or their structural transformation into blood vessels by differentiation from circulating endothelial precursors (CEPs) or by inhibiting either tube formation or the needed branching. Hence, antagonizing one ore more of these factors can inhibit the development and

progression of cancer and inflammatory disease. As described herein, CSR isoforms can be administered as therapeutics for such diseases and conditions.

L. Exemplary Treatments and Studies with CSR isoforms

Provided herein are methods of treatment with CSR isoforms for diseases and conditions. CSR isoforms such as RTK isoforms and TNFR isoforms can be used in the treatment of a variety of diseases and conditions, including those described herein. Treatment can be effected by administering by suitable route formulations of the polypeptides, which can be provided in compositions as polypeptides and can be linked to targeting agents, for targeted delivery or encapsulated in delivery vehicles, such as liposomes. Alternatively, nucleic acids encoding the polypeptides can be administered as naked nucleic acids or in vectors, particularly gene therapy vectors. G ene therapy can be effected by any method known to those of skill in the art. Gene therapy can be effect in vivo by directly administering the nucleic acid or vector. For example, the nucleic acids can be delivered systemically, locally, topically or by any suitable route. The vectors or nucleic acids can be targeted by including targeting agents in delivery vehicle, such as a virus or liposome, or they can be conjugated to a targeting agent, such as an antibody. The vectors or nucleic acids can be introduced into cells *ex vivo* by removing cells from a subject or suitable donor, introducing the vector or nucleic acid into the cells and then introducing the modified cells into the subject.

The CSR isoforms provided herein can be used for treating a variety of disorders, particularly proliferative, immune and inflammatory disorders. Treatments, include, but are not limited to treatment of angiogenesis-related diseases and conditions including ocular diseases, atherosclerosis, cancer and vascular injuries, neurodegenerative diseases, including Alzheimer's disease, inflammatory diseases and conditions, including atherosclerosis, diseases and conditions associated with cell proliferation including cancers, and smooth muscle cell-associated conditions, and various autoimmune diseases. Exemplary treatments and preclinical studies are described for treatments and therapies with RTK and TNFR isoforms. Such descriptions are meant to be exemplary only and are not limited to a particular RTK or TNFR isoform. The particular treatment and dosage can be determined by nne of

skill in the art. Considerations in assessing treatment include, the disease to be treated, the severity and course of the disease, whether the molecule is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to therapy, and the discretion of the attending physician.

1. Angiogenesis-related conditions

RTK isoforms including, but not limited to, VEGFR, PDGFR, TIE/TEK, EGFR, and EphA and TNFR isoforms including TNFR1 and TNFR2 can be used in treatment of angiogenesis- related diseases and conditions, such as ocular diseases and conditions, including ocular diseases involving neovascularization. Ocular neovascular disease is characterized by invasion of new blood vessels into the structures of the eye, such as the retina or cornea. It is the most common cause of blindness and is involved in approximately twenty eye diseases. In age-related macular degeneration, the associated visual problems are caused by an ingrowth of choroidal capillaries through defects in Bruch's membrane with proliferation of fibrovascular tissue beneath the retinal pigment epithelium. Angiogenic damage also is associated with diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma and retrolental fibroplasia. Other diseases associated with corneal neovascularization include, but are not limited to, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogrens, acne rosacea, phylectenulosis, syphilis, Mycobacteria infections, lipid degeneration, chemical bums, bacterial ulcers, fungal ulcers, Herpes simplex infections, Herpes zoster infections, protozoan infections, Karposi sarcoma, Mooren ulcer, Terrien's marginal degeneration, marginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegeners sarcoidosis, Scleritis, Steven's Johnson disease, periphigoid radial keratotomy, and corneal graph rejection. Diseases associated with retinal/choroidal neovascularization include, but are not limited to, diabetic retinopathy, macular degeneration, sickle cell anemia, sarcoid, syphilis, pseudoxanthoma elasticum, Pagets disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis/vitritis, mycobacterial infections, Lyme's disease, systemic lupus erythematosus, retinopathy of prematurity, Eales disease, Bechets disease, infections

causing a retinitis or choroiditis, presumed ocular histoplasmosis, Bests disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, trauma and post-laser complications. Other diseases include, but are not limited to, diseases associated with rubeosis (neovascularization of the angle) and diseases caused by the abnormal proliferation of fibrovascular or fibrous tissue including all forms of proliferative vitreoretinopathy.

RTK and TNFR isoform therapeutic effects on angiogenesis such as in treatment of ocular diseases can be assessed in animal models, for example in cornea implants, such as described herein. For example, modulation of angiogenesis such as for an RTK can be assessed in a nude mouse model such as epidermoid A431 tumors in nude mice and VEGF-or PIGF-transduced rat C6 gliomas implanted in nude mice. CSR isoforms can be injected as protein locally or systemically, Alternatively cells expressing CSR isoforms can be inoculated locally or at a site remote to the tumor. Tumors can be compared between control treated and CSR isoform treated models to observe phenotypes of tumor inhibition including poorly vascularized and pale tumors, necrosis, reduced proliferation and increased tumor-cell apoptosis. In one such treatment, Flt-1 isoforms are used to treat ocular disease and assessed in such models.

Examples of ocular disorders that can be treated with TIE/TEK isoforms are eye diseases characterized by ocular neovascularization including, but not limited to, diabetic retinopathy (a major complication of diabetes), retinopathy of prematurity (this devastating eye condition, that frequently leads to chronic vision problems and carries a high risk of blindness, is a severe complication during the care of premature infants), neovascular glaucoma, retinoblastoma, retrolental fibroplasia, rubeosis, uveitis, macular degeneration, and corneal graft neovascularization. Other eye inflammatory diseases, ocular tumors, and diseases associated with choroidal or iris neovascularization also can be treated with TIE/TEK isoforms.

PDGFR isoforms also can be used in the treatment of proliferative vitreoretinopathy. For example, an expression vector such as a retroviral vector is constructed containing a nucleic acid molecule encoding a PDGFR isoform. Rabbit conjunctival fibroblasts (RCFs) are produced which contain the expression vector by

transfection, such for a retrovirus vector, or by transformation, such as for a plasmid or chromosomal based vector. Expression of PDGFR isoform can be monitored in cells by means known in the art including use of an antibody which recognizes PDGFR isoform and by use of a peptide tag (*e.g.* a myc tag) and corresponding antibody. RCFs are injected into the vitreous part of an eye. For example, in a rabbit animal model, approximately 1 x 10^5 RCFs are injected by gas vitreomy. Retrovirus expressing PDGFR isoform, ~ 2 x 10^7 CFU is injected on the same day. Effects on proliferative vitreoretinopathy can be observed, for example, 2-4 weeks following surgery, such as attenuation of the disease symptoms.

EphA isoforms can be used to treat diseases or conditions with misregulated and/or inappropriate angiogenesis, such as in eye diseases. For example, an EphA isoform can be assessed in an animal model such as a mouse corneal model for effects on ephrinA-1 induced angiogenesis. Hydron pellets containing ephrinA-1 alone or with EphA isoform protein are implanted in mouse cornea. Visual observations are taken on days following implantation to observe EphA isoform inhibition or reduction of angiogenesis. Anti-angiogenic treatments and methods such as described for VEGFR isoforms are applicable to EphA isoforms.

2. Angiogenesis related atherosclerosis

RTK isoforms, for example VEGFR Flt-1 and TIE/TEK isoforms, can be used to treat angiogenesis conditions related to atherosclerosis such as neovascularization of atherosclerosis plaques. Plaques formed within the lumen of blood vessels have been shown to have angiogenic stimulatory activity. VEGF expression in human coronary atherosclerotic lesions is associated with the progression of human coronary atherosclerosis.

Animal models can be used to assess RTK isoforms in treatment of atherosclerosis. Apolipoprotein-E deficient mice ($ApoE^{-/-}$) are prone to atherosclerosis. Such mice are treated by injecting an RTK isoform, for example a VEGFR isoform, such as a Flt-1 intron fusion protein over a time course such as for 5 weeks starting at 5, 10 and 20 weeks of age. Lesions at the aortic root are assessed between control $ApoE^{-/-}$ mice and isoform-treated $ApoE^{-/-}$ mice to observe reduction of atherosclerotic lesions in isoform-treated mice.

3. Additional Angiogenesis-related treatments

RTK isoforms such as VEGFR isoforms, for example, Flt1 isoforms, and EphA isoforms also can be used to treat angiogenic and inflammatory-related conditions such as proliferation of synoviocytes, infiltration of inflammatory cells, cartilage destruction and pannus formation, such as are present in rheumatoid arthritis (RA). An autoimmune model of collagen type- II induced arthritis, such as polyarticular arthritis induced in mice, can be used as a model for human RA. Mice treated with a VEGFR isoform, such as by local injection of protein, can be observed for reduction of arthritic symptoms including paw swelling, erythema and ankylosis. Reduction is synovial angiogenesis and synovial inflammation also can be observed.

Other angiogenesis-related conditions amenable to treatment with VEGFR isoforms include hemangioma. One of the most frequent angiogenic diseases of childhood is the hemangioma. In most cases, the tumors are benign and regress without intervention. In more severe cases, the tumors progress to large cavernous and infiltrative forms and create clinical complications. Systemic forms of hemangiomas, the hemangiomatoses, have a high mortality rate. Many cases of hemangiomas exist that cannot be treated or are difficult to treat with therapeutics currently in use.

VEGFR isoforms can be employed in the treatment of such diseases and conditions where angiogenesis is responsible for damage such as in Osler-Weber-Rendu disease, or hereditary hemorrhagic telangiectasia. This is an inherited disease characterized by multiple small angiomas, tumors of blood or lymph vessels. The angiomas are found in the skin and mucous membranes, often accompanied by epistaxis (nosebleeds) or gastrointestinal bleeding and sometimes with pulmonary or hepatic arteriovenous fistula. Diseases and disorders characterized by undesirable vascular permeability also can be treated by VEGFR isoforms. These include edema associated with brain tumors, ascites associated with malignancies, Meigs' syndrome, lung inflammation, nephrotic syndrome, pericardial effusion and pleural effusion.

Angiogenesis also is involved in normal physiological processes such as reproduction and wound healing. Angiogenesis is an important step in ovulation and also in implantation of the blastula after fertilization. Modulation of angiogenesis by VEGFR isoforms can be used to induce amenorrhea, to block ovulation or to prevent

implantation by the blastula. VEGFR isoforms also can be used in surgical procedures. For example, in wound healing, excessive repair or fibroplasia can be a detrimental side effect of surgical procedures and may be caused or exacerbated by angiogenesis. Adhesions are a frequent complication of surgery and lead to problems such as small bowel obstruction.

PDGFR isoforms can be used in the regulation of neointima formation after arterial injury such as in arterial surgery. For example PDGFR-B isoforms can be used to regulate PDGF-BB induced cell proliferation such as involved in neointima formation. PDGFR isoforms can be assessed for example, in a balloon-injured rooster femoral artery model. An adenovirus vector expressing a PDGFR isoform is constructed and transduced *in vivo* in the arterial model. Neointima-associated thrombosis is assessed in the transduced arteries to observe reduction compared with controls.

RTK isoforms useful in treatment of angiogenesis-related diseases and conditions also can be used in combination therapies such as with anti-angiogenesis drugs, molecules which interact with other signaling molecules in RTK-related pathways, including modulation of VEGFR ligands. For example, the known anti-rheumatic drug, bucillamine (BUC), was shown to include within its mechanism of action the inhibition of VEGF production by synovial cells. Anti-rheumatic effects of BUC are mediated by suppression of angiogenesis and synovial proliferation in the arthritic synovium through the inhibition of VEGF production by synovial cells. Combination therapy of such drugs with VEGFR isoforms can allow multiple mechanisms and sites of action for treatment.

4. Cancers

RTK isoforms such as isoforms of EGFR, TIE/TEK, VEGFR and FGFR can be used in treatment of cancers. RTK isoforms including, but not limited to, EGFR RTK isoforms, such as ErbB2 and ErbB3 isoforms, VEGFR isoforms such as Flt1 isoforms, FGFR isoforms such as FGFR-4 isoforms, and EphA1 isoforms can be used to treat cancer. Examples of cancer to be treated herein include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia or lymphoid malignancies. Additional examples of such cancers include squamous cell cancer (e.g. epithelial

squamous cell cancer), lung cancer including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, as well as head and neck cancer. Combination therapies can be used with EGFR isoforms including anti-hormonal compounds, cardioprotectants, and anti-cancer agents such as chemotherapeutics and growth inhibitory agents.

Cancers treatable with EGFR isoforms generally are those that expressing an EGFR receptor or a receptor with which an EGF ligand interacts. Such cancers are known to those of skill in the art and/or can be identified by any means known in the art for detecting EGFR expression. An example of an ErbB2 expression diagnostic/prognostic assay available includes HERCEPTEST.RTM. (Dako). Paraffin embedded tissue sections from a tumor biopsy are subjected to the IHC assay and accorded a ErbB2 protein staining intensity criteria. Tumors accorded with less than a threshold score can be characterized as not overexpressing ErbB2, whereas those tumors with greater than or equal to a threshold score can be characterized as overexpressing ErbB2. In one example of treatment, ErbB2-overexpressing tumors are assessed as candidates for treatment with an EGFR isoform such as an ErbB2 isoform.

Isoforms provided herein can be used for treatment of cancers. For example, TIE/TEK isoforms can be used in the treatment of cancers such as by modulating tumor-related angiogenesis. Vascularization is involved in regulating cancer growth and spread. For example, inhibition of angiogenesis and neovascularization inhibits solid tumor growth and expansion. Tie/Tek receptors such as TEK have been shown to influence vascular development in normal and cancerous tissues. TIE/TEK isoforms can be used as an inhibitor of tumor angiogenesis. A TIE/TEK isoform is produced such as by expression of the protein in cells. For example, secreted forms

of TIE/TEK isoform can be expressed in cells and harvested from the media. Protein can be purified or partially-purified by biochemical means known in the art and by uses of antibody purification, such as antibodies raised against TIE/TEK isoform or a portion thereof or by use of a tagged TIE/TEK isoform and a corresponding antibody. Effects on angiogenesis can be monitored in an animal model such as by treating rat cornea with TIE/TEK isoform formulated as conditioned media in hydron pellets surgically implanted into a micropocket of a rat cornea or as purified protein *(e.g.* 100 μg/dose) administered to the window chamber. For example, rat models such as F344 rats with avascular corneas can be used in combination with tumor-cell conditioned media or by implanting a fragment of a tumor into the window chamber of an eye to induce angiogenesis. Corneas can be examined histologically to detect inhibition of angiogenesis induced by tumor-cell conditioned media. TIE/TEK isoforms also can be used to treat malignant and metastatic conditions such as solid tumors, including primary and metastatic sarcomas and carcinomas.

FGFR-4 isoforms can be used to treat cancers, for example pituitary tumors. Animal models can be used to mimic progression of human pituitary tumor progress. For example, an N-terminally shortened form of FGFR, ptd-FGFR-4, expressed in transgenic mice recapitulates pituitary tumorigenesis (Ezzat *et al.* (2002) *J. Clin. Invest. 109*:69-78), including pituitary adenoma formation in the absence of prolonged and massive hyperplasia. FGFR-4 isoforms can be administered to ptd-FGFR-4 mice and the pituitary architecture and course of tumor progression compared with control mice.

5. Alzheimer's disease

Receptor isoforms, such as EGFR isoforms, also can be used to treat inflammatory conditions and other conditions involving such responses, such as Alzheimer's disease and related conditions. A variety of mouse models are available for human Alzheimer's disease including transgenic mice overexpressing mutant amyloid precursor protein and mice expressing familial autosomal dominant-linked PS1 and mice expressing both proteins (PS1 M146L/APPK670N:M671L). Alzheimer's models are treated such as by injection of ErbB isoforms. Plaque development can be assessed such as by observation of neuritic plaques in the

hippocampus, entorhinal cortex, and cerebral cortex, using staining and antibody immunoreactivity assays.

6. Smooth Muscle Proliferative-related diseases and conditions

CSR isoforms, including EGFR isoforms, such as ErbB isoforms, can be employed for the treatment of a variety of diseases and conditions involving smooth muscle cell proliferation in a mammal, such as a human. An example is treatment of cardiac diseases involving proliferation of vascular smooth muscle cells (VSMC) and leading to intimal hyperplasia such as vascular stenosis, restenosis resulting from angioplasty or surgery or stent implants, atherosclerosis and hypertension. In such conditions, an interplay of various cells and cytokines released act in autocrine, paracrine or juxtacrine manner, which result in migration of VSMCs from their normal location in media to the damaged intima. The migrated VSMCs proliferate excessively and lead to thickening of intima, which results in stenosis or occlusion of blood vessels. The problem is compounded by platelet aggregation and deposition at the site of lesion. Alpha-thrombin, a multifunctional serine protease, is concentrated at sites of vascular injury and stimulates VSMC proliferation. Following activation of this receptor, VSMCs produce and secrete various autocrine growth factors, including PDGF-AA, HB-EGF and TGF. EGFRs are involved in signal transduction cascades that ultimately result in migration and proliferation of fibroblasts and VSMCs, as well as stimulation of VSMCs to secrete various factors that are mitogenic for endothelial cells and induction of chemotactic responses in endothelial cells. Treatment with EGFR isoforms can be used to modulate such signaling and responses.

EGFR isoforms such as ErbB2 and ErbB3 isoforms can be used to treat conditions where EGFRs such as ErbB2 and ErbB3 modulate bladder SMCs, such as bladder wall thickening that occurs in response to obstructive syndromes affecting the lower urinary tract. EGFR isoforms can be used in controlling proliferation of bladder smooth muscle cells, and consequently in the prevention or treatment of urinary obstructive syndromes.

EGFR isoforms can be used to treat obstructive airway diseases with underlying pathology involving smooth muscle cell proliferation. One example is

asthma which manifests in airway inflammation and bronchoconstriction. EGF has been shown to stimulate proliferation of human airway SMCs and is likely to be one of the factors involved in the pathological proliferation of airway SMCs in obstructive airway diseases. EGFR isoforms can be used to modulate effects and responses to EGF by EGFRs.

7. Inflammatory diseases

CSR isoforms such as TNFR isoforms can be used in the treatment of inflammatory diseases including central nervous system diseases (CNS), autoimmune diseases, airway hyper-responsiveness conditions such as in asthma, rheumatoid arthritis and inflammatory bowel disease.

TNF α and LT are proinflammatory cytokines and critical mediators in inflammatory responses in diseases and conditions such as multiple sclerosis. TNF α and LT-α are produced by infiltrating lymphocytes and macrophages and additionally by activated CNS parenchymal cells, microglial cells and astrocytes. In MS patients, TNF-α is overproduced in serum and cerebrospinal fluid. In lesions, TNF-α and TNFR are extensively expressed. TNF α and LT-α can induce selective toxicity of primary oligodendrocytes and induce myelin damage in CNS tissues. Thus, these two cytokines have been implicated in demyelination.

Experimental autoimmune encephalomyelitis (EAE) can serve as a model for multiple sclerosis (MS) (see for example, Probert *et al.* (2000) *Brain 123*: 2005-2019). 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 of the pathohistological triad of inflammation, reactive gliosis, and the formation of large confluent demyelinated plaques. Additional MS models include transgenic mice overexpressing TNF α, which model non-autoimmune mediated MS. Transgenic mice are engineered to express TNF α locally in glial cells; human and murine TNF α trigger MS-like symptoms. TNFR isoforms can be assessed in EAE animal models. Isoforms are administered, such as

by injection, and the course and progression of symptoms is monitored compared to control animals.

Cytokines such as TNF α also are involved in airway smooth muscle contractile properties. TNFR1 and TNFR2 play a role in modulating biological affects in airway smooth muscle. TNFR2 modulates calcium homeostasis and thereby modulates airway smooth muscle hyper-responsiveness. TNFR1 modulates effects of TNF α in airway smooth muscle. Airway smooth muscle responses can be assessed in murine tracheal rings induced with carbachol. Effects, such as carbachol-induced contraction, in the presence and absence of TNF α can be monitored. TNFR isoforms can be added to tracheal rings to assess the effects of isoforms on airway smooth muscle.

TNF α/TNFRs modulate inflammation in diseases such as rheumatoid arthritis (RA) (Edwards *et al.* (2003) *Adv Drug Deliv. Rev. 55(10)*:1315-36). TNFR isoforms, including TNFR1 isoforms, can be used to treat RA. For example, TNFR isoforms can be injected locally or systemically. Isoforms can be dosed daily or weekly. PEGylated TNFR isoforms can be used to reduce immunogenicity. Primate models are available for RA treatments. Response of tender and swollen joints can be monitored in subjects treated with TNFR isoforms and controls to assess TNFR isoform treatment.

8. Combination Therapies

CSR isoforms such as RTK isoforms can be used in combination with each other and with other existing drugs and therapeutics to treat diseases and conditions. For example, as described herein a number of RTK-isoforms can be used to treat angiogenesis-related conditions and diseases and/or control tumor proliferation. Such treatments can be performed in conjunction with anti-angiogenic and/or anti-tumorigenic drugs and/or therapeutics. Examples of anti-angiogenic and anti-tumorigenic drugs and therapies useful for combination therapies include tyrosine kinase inhibitors and molecules capable of modulating tyrosine kinase signal transduction including, but not limited to, 4-aminopyrrolo[2,3-d]pyrimidines (see for example, U.S. Pat. No. 5,639,757), and quinazoline compounds and compositions (*e.g.*, U.S. Pat. No. 5,792,771). Other

compounds useful in combination therapies include steroids such as the angiostatic 4,9(11)-steroids and C21-oxygenated steroids, angiostatin, endostatin, vasculostatin, canstatin and maspin, angiopoietins, bacterial polysaccharide CM101 and the antibody LM609 (U.S. Pat. No. 5,753,230), thrombospondin (TSP-1), platelet factor 4 (PF4), interferons, metalloproteinase inhibitors, pharmacological agents including AGM-1470/TNP-470, thalidomide, and carboxyamidotriazole (CAI), cortisone such as in the presence of heparin or heparin fragments, anti-Invasive Factor, retinoic acids and paclitaxel (U.S. Pat. No. 5,716,981; incorporated herein by reference), shark cartilage extract, anionic polyamide or polyurea oligomers, oxindole derivatives, estradiol derivatives and thiazolopyrimidine derivatives.

Treatment of cancers including treatment of cancers overexpressing an EGFR can include combination therapy with an anticancer agent, a chemotherapeutic agent and growth inhibitory agent, including coadministration of cocktails of different chemotherapeutic agents. Examples of chemotherapeutic agents include taxanes (such as paclitaxel and doxetaxel) and anthracycline antibiotics. Preparation and dosing schedules for such chemotherapeutic agents may be used according to manufacturers' instructions or as determined empirically by the skilled practitioner. Preparation and dosing schedules for such chemotherapy also are described in Chemotherapy Service Ed., M. C. Perry, Williams & Wilkins, Baltimore, Md. (1992).

Additional compounds can be used in combination therapy with RTK isoforms. Anti-hormonal compounds can be used in combination therapies, such as with EGFR isoforms. Examples of such compounds include an anti-estrogen compound such as tamoxifen; an anti-progesterone such as onapristone and an anti-androgen such as flutamide, in dosages known for such molecules. It also can be beneficial to also coadminister a cardioprotectant (to prevent or reduce myocardial dysfunction that can be associated with therapy) or one or more cytokines. In addition to the above therapeutic regimes, the patient may be subjected to surgical removal of cancer cells and/or radiation therapy.

Adjuvants and other immune modulators can be used in combination with CSR isoforms in treating cancers, for example to increase immune response to tumor cells. Combination therapy can increase the effectiveness of treatments and in some

cases, create synergistic effects such the combination is more effective than the additive effect of the treatments separately. Examples of adjuvants include, but are not limited to, bacterial DNA, nucleic acid fraction of attenuated mycobacterial cells (BCG; Bacillus-Calmette-Guerin), synthetic oligonucleotides from the BCG genome, and synthetic oligonucleotides containing CpG motifs (CpG ODN; Wooldridge *et al.* (1997) *Blood 89*:2994-2998), levamisole, aluminum hydroxide (alum), BCG, Incomplete Freud's Adjuvant (IFA), QS-21 (a plant derived immunostimulant), keyhole limpet hemocyanin (KLH), and dinitrophenyl (DNP). Examples of immune modulators include but are not limited to, cytokines such as interleukins (*e.g.*, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, IL-17, IL-18, IL-1α, IL-1β, and IL-1 RA), granulocyte colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), oncostatin M, erythropoietin, leukemia inhibitory factor (LIF), interferons, B7.1 (also known as CD80), B7.2 (also known as B70, CD86), TNF family members (TNF- α, TNF-β, LT-β, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, 4-1BBL, Trail), and MIF, interferon, cytokines such as IL-2 and IL-12; and chemotherapy agents such as methotrexate and chlorambucil.

9. Preclinical studies

Model animal studies can be used in preclinical evaluation of RTK isoforms that are candidate therapeutics. Parameters that can be assessed include, but are not limited to efficacy and concentration-response, safety, pharmacokinetics, interspecies scaling and tissue distribution. Model animal studies include assays such as described herein as well as those known to one of skill in the art. Animal models can be used to obtain data that then can be extrapolated to human dosages for design of clinical trials and treatments with RTK isoforms. For example, efficacy and concentration-response VEGFR inhibitors in tumor-bearing mice can be extrapolated to human treatment (Mordenti *et al.*, (1999) *Toxicol Pathol. Jan-Feb;27(1)*:14-21) in order to define clinical dosing regimens effective to maintain a therapeutic inhibitor, such as an antibody against VEGFR for human use in the required efficacious range. Similar models and dose studies can be applied to VEGFR isoform dosage determination and translation into appropriate human doses, as well as other techniques known to the

skilled artisan. Preclinical safety studies and preclinical pharmacokinetics can be performed, for example in monkeys, mice, rats and rabbits. Pharmacokinetic data from mice, rats and monkeys has been used to predict the pharmacokinetics of the counterpart therapeutic in human using allometric scaling. Accordingly, appropriate dosage information can be determined for the treatment of human pathological conditions, including rheumatoid arthritis, ocular neovascularization and cancer. A humanized version of the anti-VEGF antibody has been employed in clinical trials as an anti-cancer agent (Brem, (1998) *Cancer Res. 58(13)*:2784-92; Presta *et al.*, (1997) *Cancer Res. 57(20)*:4593-9) and such clinical data also can be considered as a reference source when designing therapeutic doses for VEGFR isoforms.

M. Combination Therapies

CSR isoforms, including those provided herein , can be used in combination with each other, with other cell surface receptor isoforms, such as a herstatin or any described, for example, in U.S. Application Serial Nos. 09/942,959, 09/234,208, 09/506,079; U.S. Provisional Application Serial Nos. 60/571,289, 60/580,990 and 60/666,825; and U.S. Patent No. 6,414,130, published International PCT application No. WO 00/44403, WO 01/61356, WO 2005/016966, including but not limited to, those set forth in SEQ ID Nos. 320-359; and/or with other existing drugs and therapeutics to treat diseases and conditions, particularly those involving aberrant angiogenesis and/or neovascularization, including, but not limited to, cancers and other proliferative disorders, inflammatory diseases, autoimmune disorders, as set forth herein and known to those of skill in the art.

For example, a CSR isoform, such as a VEGF isoform, can be administered with an agent for treatment of diabetes. Such agents include agents for the treatment of any or all conditions such as diabetic periodontal disease, diabetic vascular disease, tubulointerstitial disease and diabetic neuropathy. In another example, a CSR isoform is administered with an agent that treats cancers including squamous cell cancer (*e.g.* epithelial squamous cell cancer), lung cancer including small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung and squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer including gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer,

ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, as well as head and neck cancer. Any of the CSR isoforms can be administered in combination with two or more agents for treatment of a disease or a condition.

Adjuvants and other immune modulators can be used in combination with isoforms in treating cancers, for example to increase immune response to tumor cells. Combination therapy can increase the effectiveness of treatments and in some cases, create synergistic effects such the combination is more effective than the additive effect of the treatments separately. Examples of adjuvants include, but are not limited to, bacterial DNA, nucleic acid fraction of attenuated mycobacterial cells (BCG; Bacillus-Calmette-Guerin), synthetic oligonucleotides from the BCG genome, and synthetic oligonucleotides containing CpG motifs (CpG ODN; Wooldridge et al. (1997) Blood 89:2994-2998), levamisole, aluminum hydroxide (alum), BCG, Incomplete Freud's Adjuvant (IFA), QS-21 (a plant derived immunostimulant), keyhole limpet hemocyanin (KLH), and dinitrophenyl (DNP). Examples of immune modulators include but are not limited to, cytokines such as interleukins (*e.g.*, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, IL-17, IL-18, IL-1α, IL-1β, and IL-1 RA), granulocyte colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), oncostatin M, erythropoietin, leukemia inhibitory factor (LIF), interferons, B7.1 (also known as CD80), B7.2 (also known as B70, CD86), TNF family members (TNF- α, TNF-β, LT-β, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, 4-1BBL, Trail), and MIF, interferon, cytokines such as IL-2 and IL-12; and chemotherapy agents such as methotrexate and chlorambucil.

Combinations of different CSR isoforms including with herstatins and other agents, can be used for treating cancers and other disorders involving aberrant angiogenesis (see, *e.g.* Fig.1 outlining targets in the angiogenesis and neovascularization pathway for such polypeptides and those described herein and in the above-noted copending and published applications U.S. Application Serial Nos. 09/942,959,

09/234,208, 09/506,079; U.S. Provisional Application Serial Nos. 60/571,289, 60/580,990 and 60/666,825; and U.S. Patent No. 6,414,130, published International PCT application No. WO 00/44403, WO 01/61356, WO 2005/016966 are provided. The cell surface receptors include receptor tyrosine kinases, such as members of the VEGFR, FGFR, PDGFR (including Rα, Rβ, CSF1R, Kit), Met (including c-Met, c-RON), TEK and EphA2 families. These also include ErbB2, ErbB3, ErbB4, DDR1, DDR2, EphA, EphB, FGFR-2, FGFR-3, FGFR-4, MET, PDGFR, TEK, Tie-1, KIT, ErbB2, VEGFR-1, VEGFR-2, VEGFR-3, Flt1, Flt3, TNFR1, TNFR2, RON, CSFR. Exemplary of such isoforms are the herstatins (see, SEQ ID Nos. 320-345), polypeptides that include the intron portion of a herstatin as well as any isoforms provided herein. The combinations of isoforms and/or drug agent selected is a function of the disease to be treated and is based upon consideration of the target tissues and cells and receptors expressed thereon.

The combinations, for example, can target two or more cell surface receptors or steps in the angiogenic and/or endothelial cell maintenance pathways or can target two or more cell surface receptors or steps in a disease process, such as any which one or both of these pathways are implicated, such as inflammatory diseases, tumors and all other noted herein and known to those of skill in the art. The two or more agents can be administered as a single composition or can be administered as two or more compositions (where there are more than two agents) simultaneously, intermittently or sequentially. They can be packaged as a kit that contains two or more compositions separately or as a combined composition and optionally with instructions for administration and/or devices for administration, such as syringes

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

N. EXAMPLES

Example 1

Method for cloning CSR isoforms

A. Preparation of messenger RNA

mRNA isolated from major human tissue types from healthy or diseased tissues or cell lines were purchased from Clontech (BD Biosciences, Clontech, Palo

Alto, CA) and Stratagene (La Jolla, CA). Equal amounts of mRNA were pooled and used as templates for reverse transcription-based PCR amplification (RT-PCR).

B. cDNA synthesis

mRNA was denatured at 70°C in the presence of 40% DMSO for 10 min and quenched on ice. First-strand cDNA was synthesized with either 200 ng oligo(dT) or 20 ng random hexamers in a 20-μl reaction containing 10% DMSO, 50 mM Tris-HCl (pH 8.3), 75 mM KCl, 3 mM $MgCl_2$, 10 mM DTT, 2mM each dNTP, 5 μg mRNA, and 200 units of Stratascript reverse transcriptase (Stratagene, La Jolla, CA). After incubation at 37°C for 1 h, the cDNA from both reactions were pooled and treated with 10 units of RNase H (Promega, Madison, WI).

C. PCR amplification

Gene-specific PCR primers were selected using the Oligo 6.6 software (Molecular Biology Insights, Inc., Cascade, CO) and synthesized by Qiagen-Operon (Richmond, CA). The forward primers flank the start codon. The reverse primers flank the stop codon or were chosen from regions at least 1.5 kb downstream from the start codon (see Table 4). Each PCR reaction contained 10 ng of reverse-transcribed cDNA, 0.025 U/μl TaqPlus (Stratagene), 0.0035 U/μl PfuTurbo (Stratagene), 0.2 mM dNTP (Amersham, Piscataway, NJ), and 0.2 μM forward and reverse primers in a total volume of 50 μl. PCR conditions were 35 cycles and 94.5°C for 45 s, 58°C for 50 s, and 72°C for 5 min. The reaction was terminated with an elongation step of 72°C for 10 min.

TABLE 3B: LIST OF GENES FOR CLONING CSR Isoforms

Family	Member	nt ACC. #	Catalytic Domain	SEQ ID NO:	ORF	prt ACC.#	SEQ ID NO:
PDGFR	CSF1R	NM_005211	2012-3208	162	293-3211	NP_005202	249
	Flt3	NM_004119	1861-2886	244	58-3039	NP_004110	272
	KIT	NM_000222	1762-2799	1	22-2952	NP_000213	273
	PDGFR-A	NM_006206	2147-3253	246	395-3664	NP_006197	275
	PDGFR-B	NM_002609	2133-3215	163	357-3677	NP_002600	276
DDR	DDR1	NM_013993	2149-	156	337-	NP_054699	250

Family	Member	nt ACC. #	Catalytic Domain	SEQ ID NO:	ORF	prt ACC.#	SEQ ID NO:
			3057		3078		
	DDR2	NM_006182	2022-2900	227	354-2921	NP_006173	251
EPH	EphA1	NM-005232	1939-2736	165	88-3018	NP_005223	253
	EphA2	NM-004431	1956-2759	229	138-3068	NP_004422	254
	EphA3	NM-005233	2086-2859	230	226-3177	NP_005224	255
	EphA4	NM_004438	1885-2685	231	43-3003	NP_004429	256
	EphA5	L36644	1259-1460	232	1-2976	AAA74245	257
	EphA6	AL133666	691-1332	233	343-1347	CAB63775	258
	EphA7	NM_004440	2092-2892	234	214-3210	NP_004431	259
	EphA8	NM_020526	2028-2801	235	126-3143	NP_065387	260
	EphB1	NM_004441	2051-2857	166	215-3169	NP_004432	261
	EphB2	AF025304	1886-2681	236	26-3193	AAB94602	262
	EphB3	NM_004443	2316-3122	237	438-3434	NP_004434	263
	EphB4	NM_004444	2200-3006	238	376-3339	NP_004435	264
	EphB6	NM_004445	2761-3498	239	799-3819	NP_004436	265
ERB	ErbB2	NM_004448	2396-3164	240	239-4006	NP_004439	266
	ErbB3	NM_001982	2318-3086	241	194-4222	NP_001973	267
	EGFR	NM_005228	2380-3148	228	247-3879	NP_005219	252
FGFR	FGFR-1	M34641	1435-2263	164	10-2472	AAA35835	268
	FGFR-2	NM_000141	2009-2872	242	593-3058	NP_000132	269
	FGFR-3	NM_000142	1429-2292	243	40-2460	NP_000133	270
	FGFR-4	NM_002011	1534-2394	2	157-2565	NP_002002	271
MET	MET	NM_000245	3419-4198	245	188-4360	NP_000236	274
	RON	NM_002447	3242-4260	159	29-4231	NP_002438	277
TEK	TEK	NM_000459	2603-3433	160	149-3523	NP_000450	278
	Tie-1	NM_005424	2579-3409	161	80-3496	NP_005415	279
TNFR	TNFR1	NM_001065	1323-	247	282-	NP_001056	280

Family	Member	nt ACC. #	Catalytic Domain	SEQ ID NO:	ORF	prt ACC.#	SEQ ID NO:
			1598(DD)		1649		
	TNFR2	NM_001066	n/a	3	90-1475	NP_001057	281
VEGFR	VEGFR-1	NM_002019	2704-3702	157	250-4266	NP_002010	282
	VEGFR-2	NM_002253	2779-3792	248	304-4374	NP_002244	283
	VEGFR-3	NM_002020	2530-3525	158	22-3918	NP_002011	284

Table 4: PRIMERS FOR PCR CLONING.

SEQ ID NO	Primer	Sequence
4	CSFIR_F1	CTG CCA CTT CCC CAC CGA GG
5	DDR1_F1	GGG ATC AGG AGC TAT GGG ACC A
6	DDR2_F1	CTG AGA TGA TCC TGA TTC CCA GAA
7	EphA1_F1	GGA GCT ATG GAG CGG CGC TG
8	EphA2_F1	AGC GAG AAG CGC GGC ATG GA
9	EphA3_F1	CAC CAG CAA CAT GGA TTG TCA GC
10	EphA4_F1	CGA ACC ATG GCT GGG ATT TTC TA
11	EphA7_F1	ATA AAA CCT GCT CAT GCA CCA TG
12	EphB1_F1	GCG ATG GCC CTG GAT TAT CTA
13	EphB2_F1	CCC CGG GAA GCG CAG CCA
14	EphB3_F1	GCT CCT AGA GCT GCC ACG GC
15	EphB4_F1	GAT CCT ACC CGA GTG AGG CGG
16	CSFIR_R1	GGG CTC CTG CAG AGA TGG GTA
17	DDR1_R1	AGA GCC ATT GGG GAC ACA GGG A
18	DDR2_R1	AGC CTG ACT CCT CCT CCC CTG
19	EphA1_R1	AGC TCT GTC AGC AAG ACC CTG G
20	EphA2_R1	AGG TGG TGT CTG GGG CCA GGT C
21	EphA3_R1	GTC AGG CTT GAG GCT ACT GAT GG
22	EphA4_R1	AAC ATA GGA AGT GAG AGG GTT CAG G
23	EphA7_R1	ACT CCA TTG GGA TGC TCT GGT TC
24	EphB1_R1	AGC CCA TCA ATC CTT GCT GTG
25	EphB2_R1	GCG TGC CCG CAC CTG GAA GA
26	EphB3_R1	GCT GGT CAC TGT GGA GGC GA
27	EphB4_R1	GGT AGC TGG CTC CCC GCT TCA
28	CSFIR_R2	CCG AGG GTC TTA CCA AAC TGC
29	DDR1_R2	AAG CGG AGT CGA GAT CGA GGG A
30	DDR2_R2	GGG GAA CTC CTC CAC AGC CA
31	EphA1_R2	CGG GTA AAG TCC AAG GCT CCC
32	EphA2_R2	GAC ACA GGA TGG ATG GAT CTC GG
33	EphA3_R2	ATC AAT GGA TAT GTT GGT GGC ATC
34	EphA4_R2	AGG ATG CGT CAA TTT CTT TGG CA

SEQ ID NO	Primer	Sequence
35	EphA7_R2	CTG CAC CAA TCA CAC GCT CAA
36	EphB1_R2	ATC AAT CTC CTT GGC AAA CTC C
37	EphB2_R2	GCC CAT GAT GGA GGC TTC GC
38	EphB3_R2	ACG CAG GAC ACG TCG ATC TCC
39	EphB4_R2	ACC TGC ACC AAT CAC CTC TTC AA
40	EphB6_F1	AGA GTG GCG GGC ATG GTG TG
41	EphB6_R1	GCG GAG CTG ATA GTC CAG GAT G
42	EphB6_R2	CCT GTC CCA ATG ACC TCC TCA A
43	EphA6_F1	GGA GAT GAA AGA CTC TCC ATT TCA AG
44	FGFR-1_F1	ATT CGG GAT GTG GAG CTG GA
45	FGFR-2_F1	AGG ACC GGG GAT TGG TAC CG
46	FGFR-3_F1	CAT GGG CGC CCC TGC CTG
47	FGFR-4_F1	AGA AGG AGA TGC GGC TGC TG
48	TNFR1 (p55)_F1	AGC TGT CTG GCA TGG GCC TCT C
49	TNFR2 (p75)_F1	ACC GGA CCC CGC CCG CAC
50	EphA6_R1	ATCT TAG ACC GAC AGA AAA TTT GGC
51	FGFR-1_R1	CAA GGG ACC ATC CTG CGT GC
52	FGFR-2_R1	AGG GGC TTG CCC AGT GTC AG
53	FGFR-3_R1	GCT CCC ATT TGG GGT CGG CA
54	FGFR-4_R1	CGG GGG AAC TCC CAT AGT GG
55	TNFR1 (p55)_R1	GGC GCA GCC TCA TCT GAG AAG A
56	TNFR2 (p75)_R1	CAC AGC CCA CAC CGG CCT GG
57	Flt3_F1	GGA GGC CAT GCC GGC GTT G
58	KIT-F1	CGC AGC TAC CGC GAT GAG AGG
59	MET_F1	CTC ATA ATG AAG GCC CCC GC
60	PDGFR-A_F1	AAG TTT CCC AGA GCT ATG GGG A
61	PDGFR-B_F1	AGC AGC AAG GAC ACC ATG CG
62	RON_F1	GGT CCC AGC TCG CCT CGA TG
63	TEK_F1	AGA TTT GGG GAA GCA TGG ACT C
64	Tie-1_F1	CGG CCT CTG GAG TAT GGT CTG
65	VEGFR-1_F1	CAT GGT CAG CTA CTG GGA CAC C
66	VEGFR-2_F1	AGG TGC AGG ATG CAG AGC AAG
67	VEGFR-3_F1	AGC GGC CGG AGA TGC AGC G
68	Flt3_R1	CTG CTC GAC ACC CAC TGT CCA
69	KIT-R1	GCA GAA GTC TTG CCC ACA TCG
70	MET_R1	CTT CGT GAT CTT CTT CCC AGT GA
71	PDGFR-A_R1	AGA TTC TTA GCC AGG CAT CGC A
72	PDGFR-B_R1	AGC GCA CCG ACA GTG GCC GA
73	RON_R1	GCA CGG GCT GCC CAC TGT CA
74	TEK_R1	CTG TCC GAG GTT CCA AAT AGT TGA
75	Tie-1_R1	CGT TCT CAC TGG GGT CCA CCA
76	VEGFR-1_R1	ATT ATT GCC ATG CGC TGA GTG A
77	VEGFR-2_R1	GCC GCT TGG ATA ACA AGG GTA
78	VEGFR-3_R1	AAC TCG GTC CAG GTG TCC AGG C
79	Flt3_R2	CTT GGA AAC TCC CAT TTG AGA TCA
80	KIT-R2	ACA ACC TTC CCG AAA GCT CCA
81	MET_R2	ACT ACA TGC TGC ACT GCC TGG A
82	PDGFR-A_R2	CCC GAC CAA GCA CTA GTC CAT C

SEQ ID NO	Primer	Sequence
83	PDGFR-B_R2	CCA GAG CCG AGG GTG CGT CC
84	RON_R2	CAG GTC ATT CAG GTT GGG AGG A
85	TEK_R2	ATT TGA TGT CAT TCC AGT CAA GCA
86	Tie-1_R2	AGC ACT GGG TAG CTC AGG GGC
87	VEGFR-1_R2	AAC TCC CAC TTG CTG GCA TCA
88	VEGFR-2_R2	AAT TCC CAT TTG CTG GCA TCA
89	VEGFR-3_R2	ATT CCC ACT GGC TGG CAT CGT A

D. Cloning and sequencing of PCR products

PCR products were electrophoresed on a 1% agarose gel, and DNA from detectable bands was stained with Gelstar (BioWhitaker Molecular Application, Walkersville, MD). The DNA bands were extracted with the QiaQuick gel extraction kit (Qiagen, Valencia, CA), ligated into the pDrive UA-cloning vector (Qiagen), and transformed into *Escherichia coli*. Recombinant plasmids were selected on LB agar plates containing 100 μg/ml carbenicillin. For each transfection, 192 colonies were randomly picked and their cDNA insert sizes were determined by PCR with M13 forward and reverse vector primers. Representative clones from PCR products with distinguishable molecular masses as visualized by fluorescence imaging (Alpha Innotech, San Leandro, CA) were then sequenced from both directions with vector primers (M13 forward and reverse). All clones were sequenced entirely using custom primers for directed sequencing completion across gapped regions.

E. Sequence analysis

Computational analysis of alternative splicing was performed by alignment of each cDNA sequence to its respective genomic sequence using SIM4 (a computer program for analysis of splice variants). Only transcripts with canonical (e.g. GT-AG) donor-acceptor splicing sites were considered for analysis. Clones encoding CSR isoforms were studied further (see below, Table 5).

F. Targeted cloning and expression

Computational analysis of public EST databases identified potential splice variants with intron retention or insertion. Cloning of potential splice variants identified by EST database analysis were performed by RT-PCR using primers flanking the open reading frame as described above.

Sequence-verified CSR isoform encoding cDNA molecules were and can be subcloned into a replication-deficient recombinant adenoviral vector under control of the CMV promoter, following the manufacturer's instruction (Invitrogen, Cat# K4930-00). The recombinant adenoviruses were produced using 293A cells (Invitrogen). Supernatants from the infected 293 cells were analyzed by immunoblotting using an appropriate antibody.

G. Exemplary CSR Isoforms

Exemplary CSR isoforms, prepared using the methods described herein, are set forth below in Table 5. Nucleic acid molecules encoding CSR isoforms are provided and include those that contain sequences of nucleotides or ribonucleotides or nucleotide or ribonucleotide analogs as set forth in any of SEQ ID NOS: 92, 94, 96, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, and 225. The amino acid sequences of exemplary CSR isoform polypeptides are set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 182, 184, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, and 226.

TABLE 5 CSR Isoforms

Gene	ID	Type	Length	SEQ ID NOS
FGFR-4	SR002_A11	Intron fusion	72 aa	90-91
KIT	SR002_H01	Intron fusion	413 aa	92-93
TNFR2	SR003_H02	Intron fusion	155 aa	94-95
DDR1	SR005_A11	Exon deletion	286 aa	114-115
DDR1	SR005_A10	Exon deletion	243 aa	116-117
FGFR-1	SR001_E12	Exon deletions	228 aa	118-119
FGFR-4	SR002_A10	Intron fusion	446 aa	120-121
VEGFR-1	SR004_C05	Intron fusion	174 aa	122-123
VEGFR-3	SR007_E10	Exon short	227 aa	124-125
VEGFR-3	SR007_F05	Exon deletion	295 aa	126-127
RON	SR004_C11	Intron fusion	495 aa	128-129
TEK	SR007_G02	Intron fusion, exon shorten	367 aa	130-131
TEK	SR007_H03	Exon deletion, Intron fusion	468 aa	132-133

Gene	ID	Type	Length	SEQ ID NOS
Tie-1	SR006_A04	Intron fusion	251 aa	134-135
Tie-1	SR006_B07	Intron fusion	379 aa	136-137
Tie-1	SR006_B06	Intron fusion	161 aa	138-139
Tie-1	SR006_B12	Intron fusion	414 aa	140-141
Tie-1	SR006_B10	Exon deletion	317 aa	142-143
CSF1R	SR005_A06	Exon deletion	306 aa	144-145
PDGFR-B	SR007_C09	Exon shorten (4 bp)	336 aa	146-147
EphA1	SR004_G03	Intron fusion	474 aa	148-149
EphA1	SR004_G07	Intron fusion, exon deletion	311 aa	150-151
EphA1	SR004_H03	Intron fusion	490 aa	152-153
EphB1	SR005_D06	Exon shorten	242 aa	154-155
EphA2	SR016_E12	Intron fusion	497 aa	167-168
EphB4	SR012_C08	Exon deletion	306 aa	169-170
EphB4	SR012_D11	Exon shorten	516 aa	171-172
EphB4	SR012_E11	Exon shorted	414 aa	173-174
FGFR-1	SR022_C02	Exon deletion, intron fusion	320 aa	175-176
FGFR-2	SR022_C10	Intron fusion	266 aa	177-178
FGFR-2	SR022_C11	Intron fusion	317 aa	179-180
FGFR-2	SR022_D04	Exon deletion, intron fusion	281 aa	181-182
FGFR-2	SR022_D06	Intron fusion	396 aa	183-184
MET	SR020_C10	Intron fusion	413 aa	185-186
MET	SR020_C12	Intron fusion	468 aa	187-188
MET	SR020_D04	Intron fusion	518 aa	189-190
MET	SR020_D07	Intron fusion	596 aa	191-192
MET	SR020_D11	Intron fusion	408 aa	193-194
MET	SR020_E11	Intron fusion	621 aa	195-196
MET	SR020_F08	Intron fusion	664 aa	197-198
MET	SR020_F11	Intron fusion	719 aa	199-200
MET	SR020_F12	Intron fusion	697 aa	201-202
MET	SR020_G03	Exon shorten, intron fusion	691 aa	203-204
MET	SR020_G07	Intron fusion	661 aa	205-206
MET	SR020_H03	Intron fusion	755 aa	207-208
MET	SR020_H06	Intron fusion	823 aa	209-210
MET	SR020_H07	Intron fusion	877 aa	211-212
MET	SR020_H08	Exon deletion, intron fusion	764 aa	213-214
RON	SR014_C01	Intron fusion	541 aa	215-216
RON	SR014_C09	Intron fusion	908 aa	217-218
RON	SR014_E12	Intron fusion	647 aa	219-220
Tie-1	SR016_G03	Intron fusion	751 aa	221-222
VEGFR-1	SR01_C02	Intron fusion	541 aa	100
VEGFR-2	SR015_F01	Exon shorten	712 aa	223-224

Gene	ID	Type	Length	SEQ ID NOS
VEGFR-3	SR015_G09	Intron fusion	765 aa	225-226

Example 2

CSR Isoform expression Assays

A. Analysis of mRNA expression

Expression of the cloned CSR isoforms were determined by RT-PCR (or quantitative PCR) in various tissues including: brain, heart, kidney, placenta, prostate, spleen, spinal cord, trachea, testis, uterus, fetal brain, fetal liver, adrenal gland, liver, lung, small intestine, salivary gland, skeletal muscle, thymus, thyroid and a variety of tumor tissues including: breast, colon, kidney, lung, ovary, stomach, uterus, MDA435 and HEPG2. PCR primers (such as set forth in Example 1, Table 4) were selected within the exclusive regions of retained introns or alternative exons, such that only the soluble receptor-specific signals were amplified. Each PCR reaction was performed with 2 cycle numbers (*e.g.* 32 versus 38 cycles) for the purpose of getting semi-quantitative results. Expression of each cloned CSR isoform was compared to the expression of the corresponding wildtype membrane receptor.

EphA2 (GenBank No. NM_004431 or SEQ ID NO: 229) mRNA is highly expressed in brain, heart, kidney, placenta, prostate, spleen, spinal cord, trachea, testis, uterus, fetal brain, fetal liver, adrenal gland, liver, lung, small intestine, salivary gland, skeletal muscle, thymus, and thyroid as well as expressed in the following tumor tissues: breast, colon, kidney, lung, ovary, stomach, uterus, MDA435 and HEPG2. Soluble EphA2 (SEQ ID NO: 167) mRNA is highly expressed in the trachea, lung, small intestine, and salivary gland and to a lesser extent expressed in kidney, placenta, fetal brain, fetal liver, adrenal gland, skeletal muscle, thymus, brain, heart, spleen, spinal cord, uterus, and liver as well as highly expressed in stomach tumor and to a lesser extent in colon, kidney, lung, ovary, uterus, MDA435 and HEPG2 tumor tissues.

FGFR-4 (GenBank No. NM_002011 set forth as SEQ ID NO: 2) mRNA is expressed in a variety of human tissues, including brain, heart, kidney, placenta, prostate, spleen, spinal cord, trachea, testis, uterus, fetal brain, fetal liver, adrenal gland, liver, lung, small intestine, salivary gland, skeletal muscle, thymus, and

thyroid. FGFR-4 mRNA also is expressed in the following tumor tissues: breast, colon, kidney, lung, ovary, stomach, uterus, and HEPG2. Soluble FGFR-4 (SEQ ID NO: 120) mRNA is highly expressed in the kidney, spleen, testis, fetal brain, fetal liver, adrenal gland, liver, lung, small intestine and to a lesser extent expressed in brain, heart, placenta, prostate, spinal cord, trachea, uterus, skeletal muscle, thymus and thyroid. Soluble FGFR-4 (SEQ ID NO: 120) mRNA also is highly expressed in kidney and stomach tumor tissue and to a lesser extent in breast, colon, lung, ovary, and HEPG2 tumor tissues.

RON (GenBank No. NM_002447 set forth as SEQ ID NO:159) mRNA is highly expressed in trachea, testis, fetal brain, lung, small intestine, and thymus as well as being expressed in salivary gland, kidney, placenta, heart, prostate, thyroid and to a lesser extent brain, spleen, spinal cord, uterus, fetal liver, adrenal gland, liver, and skeletal muscle. RON mRNA also is expressed in the following tumor tissues: breast, colon, lung, ovary, stomach, HEPG2 and to a lesser extent in kidney and uterus tumor tissue. Soluble RON (SEQ ID NO:128) mRNA is highly expressed in colon and stomach tumor tissues. Soluble RON (SEQ ID NO:128) mRNA is expressed to a lesser extent in trachea, small intestine and thymus as well as in breast, lung, and ovary tumor tissues. Soluble RON (SEQ ID NO:219) mRNA is highly expressed in prostate, trachea, fetal brain, lung, small intestine, thymus as well as breast, colon, lung, ovary, and stomach tumor tissues. Soluble RON (SEQ ID NO:219) mRNA also is expressed to a lesser extent in brain, heart, kidney, placenta, spleen, spinal cord, testis, uterus, fetal liver, adrenal gland, liver, salivary gland, skeletal muscle, thyroid as well as kidney, uterus, MDA435 and HEPG2 tumor tissues. Soluble RON (SEQ ID NO:217) mRNA is highly expressed in trachea, lung, small intestine, thymus as well as breast and colon tumor tissues. Soluble RON (SEQ ID NO:217) mRNA is expressed to a lesser extent in brain, heart, kidney, placenta, prostate, spleen, testis, uterus, fetal brain, salivary gland, thyroid as well as lung, ovary, and stomach tumor tissues.

TEK (GenBank No. NM_000459 set forth as SEQ ID NO:160) mRNA is highly expressed in heart, kidney, placenta, spleen, lung as well as colon, kidney, lung, and ovary tumor tissues. TEK mRNA also is expressed to a lesser extent in

brain, prostate, spinal cord, trachea, testis, uterus, fetal brain, fetal liver, adrenal gland, liver, small intestine, skeletal muscle, thymus, thyroid as well as breast and stomach tumor tissues. Soluble TEK (SEQ ID NO:132) mRNA has low level expression in heart and kidney, as well as colon tumor tissues.

VEGFR-1 (GenBank No. NM_002019 set forth as SEQ ID NO:157) mRNA is highly expressed in brain, heart, kidney, placenta, prostate, spleen, spinal cord, testis, uterus, fetal brain, fetal liver, adrenal gland, lung, small intestine, skeletal muscle and to a lesser extent in trachea, liver, salivary gland, thymus and thyroid. VEGFR-1 mRNA also is highly expressed in colon, kidney, lung and ovary tumor tissues and to a lesser extent expressed in breast and stomach tumor tissues. Soluble VEGFR-1 (SEQ ID NO:100) mRNA has low level expression in stomach tumor tissues.

VEGFR-3 (GenBank No. NM_002020 set forth as SEQ ID NO:158) mRNA is highly expressed in heart, kidney, placenta, spleen, fetal brain, fetal liver, lung, small intestine as well as breast, colon, kidney, lung, ovary, stomach and uterus tumor tissues. VEGFR-3 (SEQ ID NO:158) mRNA is to a lesser extent expressed in brain, prostate, spinal cord, trachea, testis, uterus, adrenal gland, liver, salivary gland, skeletal muscle, thymus, thyroid. Soluble VEGFR-3 (SEQ ID NO:225) mRNA is highly expressed in placenta, adrenal gland, lung, small intestine as well as breast, kidney, lung tumor tissues. Soluble VEGFR-3 (SEQ ID NO:225) mRNA also is expressed to a lesser extent in brain, heart, kidney, prostate, spleen, spinal cord, trachea, testis, uterus, fetal brain, fetal liver, liver, salivary gland, skeletal muscle, thymus, and thyroid as well as colon, ovary, stomach, and uterus tumor tissues.

In summary, expression of mRNA was detectable for all CSR isoforms, but in general was lower than that of the membrane receptor isoforms.

B. Cell secretion of soluble receptors

Putative CSR isoforms were analyzed in cultured human cells to assess secreted isoforms. Splice variant cDNA molecules encoding candidate CSR isoforms were subcloned into a mammalian expression vector (pcDNA3.1MycHis vector (Invitrogen, Carlsbad, CA) fused in frame with the Myc-His tag at the C-terminus of the protein to facilitate their detection.

Human embryonic kidney 293T cells were seeded at 2 x 10^6 cells/well in a 6-well plate and maintained in Dulbecco's modified Eagle's medium and 10% fetal bovine serum (Invitrogen). Cells were transfected using LipofectAMINE 2000 (Invitrogen) following the manufacturer's instructions. On the day of transfection, 5 μg plasmid DNA was mixed with 15μl of LipofectAMINE 2000 in 0.5 ml of the serum-free DMEM. The mixture was incubated for 20 minutes at room temperature before it was added to the cells. Cells were incubated at 37°C in a CO_2 incubator for 48 hours. To study the transgene expression, the supernatants were collected and the cells were lysed in PBS buffer containing 0.2% of Triton X-100. Both the cell lysates and the supernatants were assayed for the transgene expression.

Ni-agarose NTA (Qiagen) was used for purifying His6-tagged proteins under native conditions following the manufacturer's instructions. Purified His6-tagged proteins were eluted and separated on SDS-polyacrylamide gels for immunoblotting using anti-Myc antibodies (both from Invitrogen). Antibodies were diluted 1:5000.

Expression of the secreted CSR isoforms was detected in cell lysates and conditioned media by Western blot using an anti-Myc antibody (Invitrogen) FGFR-4 (SEQ ID NO: 121), RON (SEQ ID NOS: 129, 216, 218, 220), VEGFR-2 (SEQ ID NO: 224), VEGFR-3 (SEQ ID NO: 127), EphA2 (SEQ ID NO:168), EphA1 (SEQ ID NOS: 153, 149), TEK (SEQ ID NOS: 131, 133), and Tie-1 (SEQ ID NO: 222) protein was detected in cell lysates and Tie-1 (SEQ ID NO: 222), VEGFR-2 (SEQ ID NO: 224), VEGFR-3 (SEQ ID NO: 127) and EphA2 (SEQ ID NO:168) protein was detected in conditioned medium.

C. Receptor binding

Co-immunoprecipitation assays were performed to show binding of CSR isoforms and secreted isoforms to their respective membrane anchored full-length receptors (see, for example, *Jin et al. J Biol Chem 2004, 279:1408* and *Jin et al. J Biol Chem 2004, 279:14179*). Human embryo kidney 293T cells were transiently transfected with the recombinant pcDNA 3.1(MycHis) plasmid expressing soluble VEGFR-3 (as described above). Forty-eight hours after transfection, conditioned medium was collected and binding of VEGF-D was assessed. Conditioned medium (100 μl) from transfected 293T cells was incubated with VEGF-D (100 ng) in the

presence or absence of 2 μg of soluble VEGFR-1-Fc or VEGFR-3-Fc (R&D Systems) for one hour. Protein complexes were immunoprecipitated with 0.2 μg/reaction of anti-VEGF-D antibodies (R&D Systems) and separated on a denaturing protein gel probed with anti-Myc antibody. The Western blot showed protein binding between sVEGF3-Myc and VEGF-D. Furthermore, 5x molar excess of a sVEGFR-3-Fc reduced binding whereas the presence of sVEGFR-1-Fc had little to no effect on binding.

D. Proliferation Assays

A biological activity of CSR isoforms was assessed by measuring their effect on cell proliferation. HUVEC cells (Clonitix) at passage 4 were seeded into DMEM/10%FBS at a density of 4,000 cells/well in a 96-well plate. Cells were treated with or without 0.5 nM of VEGF-A (R&D Systems) in the presence or absence of 2.5 nM of sVEGFR-1-Fc, 2.5 nM of sVEGFR-2-Fc, or 1.6 – 12.5 nM of the purified sVEGFR-2. The treated cells were cultured for 7 days in standard cell culture conditions. Cell proliferation was determined in triplicate samples using CyQuant Fluorescence Assay Kit (Invitrogen Catalog #C7026) according to manufacturer's instructions. 0.5 nM of VEGF-A induced HUVEC proliferation. sVEGFR-1-Fc (2.5 nM) and sVEGFR-2-Fc (2.5 nM) each inhibited VEGFA-induced HUVEC proliferation. Soluble VEGFR-2 (SEQ ID NO: 224) inhibited VEGF-A-induced HUVEC proliferation in a dose-dependent manner.

Since modifications will be apparent to those of skill in this art, it is intended that this invention be limited only by the scope of the appended claims

CLAIMS:

1. An isolated polypeptide, comprising at least one domain of an EphA receptor, wherein the polypeptide comprises an ephrin ligand binding domain and the polypeptide lacks one or more amino acids corresponding to the transmembrane domain of the EphA receptor whereby the membrane localization of the polypeptide is reduced or abolished compared to the EphA receptor.

2. The polypeptide of claim 1, wherein the EphA receptor is selected from the group consisting of EphA1, EphA2, EphA3, EphA4, EphA5, EphA6, EphA7, and EphA8.

3. The polypeptide of claim 2, wherein the EphA receptor comprises a sequence of amino acids set forth in any of SEQ ID NO: 253 – 260 or is an allelic variant thereof.

4. The polypeptide of claim 3, wherein the allelic variant comprises one or more of the allelic variations set forth in any one of SEQ ID NOS: 289-293.

5. A polypeptide of any of claims 1-4, wherein the polypeptide lacks all or part of a protein kinase domain compared to the EphA receptor.

6. The polypeptide of any of claims 1-5, wherein the polypeptide lacks all or part of a Sterile Alpha Motif domain (SAM) compared to the EphA receptor.

7. A polypeptide of claim 1, comprising at least one domain of an EphA1 receptor as set forth in SEQ ID NO:253.

8. The polypeptide of claim 7 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the EphA1 receptor.

9. The polypeptide of claim 7, wherein the polypeptide comprises at least one domain of the EphA1 receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding the EphA1 receptor.

10. The polypeptide of any of claims 7-9, wherein the polypeptide lacks one or more amino acids of a protein kinase domain of the EphA1 receptor, whereby the kinase activity of the polypeptide is reduced or abolished compared to the EphA1 receptor.

11. The polypeptide of claim 10, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 149, 151 and 153.

12. The polypeptide of claim 11 that comprises the amino acid sequence set forth in any of SEQ ID NOS: 149, 151 and 153 or is an allelic variant thereof.

13. The polypeptide of claim 12, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 289.

14. The polypeptide of any of claims 7-13, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 149, 151 and 153.

15. The polypeptide of claim 1, comprising at least one domain of an EphA2 receptor as set forth in SEQ ID NO: 254, wherein the polypeptide lacks one or more amino acids of a transmembrane domain and protein kinase domain compared to the EphA2 receptor, whereby the membrane localization and the protein kinase activity of the polypeptide are reduced or abolished compared to the EphA2 receptor.

16. The polypeptide of claim 15 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding an EphA2 receptor.

17. The polypeptide of claim 15, wherein the polypeptide comprises at least one domain of EphA2 receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding an EphA2 receptor.

18. The polypeptide of any of claims 15-17, wherein the polypeptide lacks one or more amino acids of a fibronectin domain compared to the EphA2 receptor.

19. The polypeptide of claim 18, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in SEQ ID NO: 168.

20. The polypeptide of claim 19 that comprises the amino acid sequence set forth in SEQ ID NO: 168 or an allelic variant thereof.

21. The polypeptide of claim 20, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 290.

22. The polypeptide of any of claims 15-21, wherein the polypeptide contains the same number of amino acids as set forth in the SEQ ID NO: 168.

23. An isolated polypeptide, comprising at least one domain of an EphB receptor, wherein the polypeptide lacks one or more amino acids of a transmembrane domain compared to the EphB receptor, whereby the membrane localization of the polypeptide is reduced or abolished compared to the EphB receptor.

24. The polypeptide of claim 23, wherein the EphB receptor is selected from the group consisting of EphB1, EphB2, EphB3, EphB4, EphB5, and EphB6.

25. The polypeptide of claim 24, wherein the EphB receptor comprises a sequence of amino acids as set forth in any one of SEQ ID NOS: 261-265 or an allelic variant thereof.

26. The polypeptide of claim 25, wherein the allelic variant comprises one or more of the allelic variations as set forth in any one of SEQ ID NOS: 294-298.

27. The polypeptide of any of claims 23-26, wherein the polypeptide lacks one or more amino acids of a protein kinase domain of the EphB receptor, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the EphB receptor.

28. The polypeptide of any of claims 23-27, wherein the polypeptide lacks one or more amino acids of a Sterile Alpha Motif domain (SAM) of the EphB receptor.

29. The polypeptide of any of claims 23-28, wherein the polypeptide comprises an ephrin ligand binding domain.

30. The polypeptide of any of claims 23-29, wherein the polypeptide lacks one or more amino acids of a fibronectin domain of the EphB receptor.

31. The polypeptide of any of claims 23-30, wherein the polypeptide comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the EphB receptor.

32. The polypeptide of claim 31, wherein the polypeptide comprises at least one domain of the EphB receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding the EphB receptor.

33. The polypeptide of any of claims 23-32, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 155, 170, 172 and 174.

34. The polypeptide of claim 33 that comprises the amino acid sequence as set forth in any of SEQ ID NOS: 155, 170, 172 and 174 or an allelic variant thereof.

35. The polypeptide of claim 34, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NOS: 294 or 297.

36. The polypeptide of any of claims 23-35, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 155, 170, 172 and 174.

37. An isolated polypeptide, comprising at least one domain of an FGFR-1, wherein the polypeptide comprises an immunoglobulin domain corresponding to amino acids 253 – 357 of FGFR-1 set forth in SEQ ID NO: 268 and lacks all of a transmembrane domain corresponding to amino acids 375 – 397 of the FGFR-1.

38. The polypeptide of claim 37 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the FGFR-1.

39. The polypeptide of claim 37, wherein the polypeptide comprises at least one domain of FGFR-1 operatively linked to at least one amino acid encoded by an intron of a gene encoding FGFR-1.

40. The polypeptide of any of claims 37-39, wherein the polypeptide lacks one or more amino acids of a protein kinase domain of FGFR-1, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the FGFR-1.

41. The polypeptide of any of claims 37-40, wherein the polypeptide comprises one or more amino acids of an immunoglobulin domain corresponding to amino acids 156 – 246 of FGFR-1.

42. The polypeptide of any of claims 37-41, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 119 or 176.

43. The polypeptide of claim 42 that comprises the amino acid sequence as set forth in any of SEQ ID NOS: 119 and 176 or an allelic variant thereof.

44. The polypeptide of claim 43, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 300.

45. The polypeptide of any of claims 37-44, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NOS: 119 or 176.

46. An isolated polypeptide, comprising at least one domain of an fibroblast growth factor receptor-2 (FGFR-2), wherein:

FGFR-2 comprises the sequence of amino acids set forth in SEQ ID NO: 269;

the polypeptide lacks a transmembrane domain and a protein kinase domain compared to FGFR-2, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to FGFR-2; and

the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 178, 180, 182 and 184.

47. The polypeptide of claim 46 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the FGFR-2.

48. The polypeptide of claim 46, wherein the polypeptide comprises at least one domain of FGFR-2 operatively linked to at least one amino acid encoded by an intron of a gene encoding the FGFR-2.

49. The polypeptide of any of claims 46-48, wherein the polypeptide lacks an immunoglobulin domain corresponding to amino acids 41-125 of the FGFR-2.

50. The polypeptide of any of claims 46-48 that comprises the amino acid sequence set forth in SEQ ID NOS: 178, 180, 182 or 184 or an allelic variant thereof.

51. The polypeptide of claim 50, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 301.

52. The polypeptide of any of claims 46-51, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 178, 180, 182 and 184.

53. An isolated polypeptide, comprising at least one domain of an FGFR-4, wherein the polypeptide comprises an immunoglobulin domain corresponding to amino acids 249 – 351 of the FGFR-4 set forth in SEQ ID NO: 271 and lacks a transmembrane domain and protein kinase domain of the FGFR-4, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to FGFR-4.

54. The polypeptide of claim 53 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the FGFR-4.

55. The polypeptide of claim 53, wherein the polypeptide comprises at least one domain of FGFR-4 operatively linked to at least one amino acid encoded by an intron of a gene encoding the FGFR-4.

56. The polypeptide of any of claims 53-55, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 121.

57. The polypeptide of any of claims 53-56, that comprises the amino acid sequence set forth in SEQ ID NO: 121 or an allelic variant thereof.

58. The polypeptide of claim 57, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 303.

59. The polypeptide of any of claims 53-58, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 121.

60. An isolated polypeptide, comprising at least one domain of a DDR1 as set forth in SEQ ID NO: 250, wherein the polypeptide lacks a transmembrane domain and a protein kinase domain compared to the DDR1, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to DDR1, and the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NOS: 115 or 117.

61. The polypeptide of claim 60 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the DDR1.

62. The polypeptide of claim 61, wherein the polypeptide comprises at least one domain of DDR1 operatively linked to at least one amino acid encoded by an intron of a gene encoding the DDR1.

63. The polypeptide of any of claims 60-62, that comprises the amino acid sequence set forth in SEQ ID NOS: 115 or 117 or an allelic variant thereof.

64. The polypeptide of claim 63, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 286.

65. The polypeptide of any of claims 60-64, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NOS: 115 or 117.

66. An isolated polypeptide, comprising at least one domain of a MET receptor, wherein:

the polypeptide comprises at least one domain of MET operatively linked to at least one amino acid encoded by an intron of a gene encoding MET; and

the polypeptide lacks a transmembrane domain, protein kinase domain and at least one additional domain compared to a MET receptor set forth in SEQ ID NO: 274, whereby the membrane localization and protein kinase activity of the polypeptide is reduced or abolished compared to the MET receptor.

67. The polypeptide of claim 66 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding MET.

68. The polypeptide of claim 66, wherein the polypeptide comprises at least one domain of MET operatively linked to at least one amino acid encoded by an intron of a gene encoding MET.

69. The polypeptide of any of claims 66-68, wherein the additional domain is selected from the group consisting of a Sema domain, a plexin domain and an IPT/TIG domain.

70. The polypeptide of any of claims 66-69, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214.

71. The polypeptide of any of claims 66-70, that comprises the amino acid sequence set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214 or an allelic variant thereof.

72. The polypeptide of claim 71, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 306.

73. The polypeptide of any of claims 66-72, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 186, 188, 190, 192, 196, 198, 200, 202, 204, 206, 208 and 214.

74. An isolated polypeptide, comprising at least one domain of a RON receptor, wherein:

the polypeptide comprises a plexin domain of the RON receptor as set forth in SEQ ID NO: 277; and

the polypeptide lacks a transmembrane domain of the RON receptor, whereby the membrane localization of the polypeptide is reduced or abolished compared to the RON receptor.

75. The polypeptide of claim 74 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the RON receptor.

76. The polypeptide of claim 74, wherein the polypeptide comprises at least one domain of RON operatively linked to at least one amino acid encoded by an intron of a gene encoding RON.

77. The polypeptide of any of claims 74-76, wherein the polypeptide lacks one or more amino acids of a protein kinase domain compared to the RON receptor as set forth in SEQ ID NO: 277, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the RON receptor.

78. The polypeptide of any of claims 74-77, wherein the polypeptide comprises one or more amino acids of at least one IPT/TIG domain of the RON receptor.

79. The polypeptide of any of claims 74-78, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 216, 218 and 220.

80. The polypeptide of any of claims 74-79, that comprises the amino acid sequence set forth in any of SEQ ID NOS: 216, 218 and 220 or an allelic variant thereof.

81. The polypeptide of claim 80, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 308.

82. The polypeptide of any of claims 74-81, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 216, 218 and 220.

83. An isolated polypeptide, comprising at least one domain of a TEK receptor as set forth in SEQ ID NO: 278, wherein:

the polypeptide lacks a transmembrane domain, and a protein kinase domain whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the TEK receptor; and

the polypeptide lacks one or more amino acids of at least one fibronectin domain compared to the TEK receptor.

84. The polypeptide of claim 83 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the TEK receptor.

85. The polypeptide of claim 83, wherein the polypeptide comprises at least one domain of the TEK receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding the TEK receptor.

86. The polypeptide of any of claims 83-85, wherein the fibronectin domain lacking in the polypeptide corresponds to amino acids 444 – 529, 543 – 626, or 639 – 724 of SEQ ID NO: 278.

87. The polypeptide of any of claims 83-86, wherein the polypeptide lacks one or more amino acids of the three fibronectin domains of the TEK receptor corresponding to amino acids 444 – 529, 543 – 626, and 639 – 724 of SEQ ID NO: 278.

88. The polypeptide of any of claims 83-87, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 131 and 133.

89. The polypeptide of any of claims 83-88, that comprises the amino acid sequence set forth in any of SEQ ID NOS: 131 and 133 or an allelic variant thereof.

90. The polypeptide of claim 89, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 309.

91. The polypeptide of any of claims 83-90, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 131 and 133.

92. An isolated polypeptide, comprising all or part of at least one domain of a Tie-1 receptor as set forth in SEQ ID NO: 279, wherein:

the polypeptide lacks a transmembrane domain and a protein kinase domain compared to the Tie-1 receptor, whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the Tie-1 receptor; and

the polypeptide comprises an amino acid sequence as set forth in any of SEQ ID NOS: 135, 137, 139, 141, 143 and 222 or an allelic variant thereof.

93. The polypeptide of claim 92, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 310.

94. The polypeptide of any of claims 92 and 93, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 135, 137, 139, 141, 143 and 222.

95. An isolated polypeptide, wherein:

the polypeptide comprises a sequence of amino acids that has at least 80% sequence identity with the sequence of amino acids as set forth in SEQ ID NO: 123; and

the polypeptide lacks a transmembrane domain and a protein kinase domain compared to the VEGFR-1 receptor set forth in SEQ ID NO: 282.

96. The polypeptide of claim 95, that comprises the amino acid sequence set forth in SEQ ID NO: 123 or an allelic variant thereof.

97. The polypeptide of any of claims 95-96, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 123.

98. An isolated polypeptide, comprising at least one domain of a VEGFR set forth in any of SEQ ID NOS: 283 and 284, wherein the polypeptide lacks one or more amino acids of a transmembrane domain of the VEGFR, whereby the membrane localization of the polypeptide is reduced or abolished compared to the VEGFR.

99. The polypeptide of claim 98 that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the VEGFR.

100. The polypeptide of claim 99, wherein the polypeptide comprises at least one domain of the VEGFR operatively linked to at least one amino acid encoded by an intron of a gene encoding the VEGFR.

101. The polypeptide of any of claims 98-100, wherein the polypeptide lacks one or more amino acids of a protein kinase domain, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the VEGFR.

102. The polypeptide of any of claims 98-101, wherein the polypeptide lacks one or more amino acids of an immunoglobulin domain compared to the VEGFR.

103. The polypeptide of claim 102, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids as set forth in any of SEQ ID NOS: 125, 127, 224 and 226.

104. The polypeptide of any of claims 99-103, that comprises the amino acid sequence set forth in any of SEQ ID NOS: 125, 127, 224 and 226 or an allelic variant thereof.

105. The polypeptide of claim 104, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NOS: 313 or 314.

106. The polypeptide of any of claims 99-105, wherein the polypeptide contains the same number of amino acids as set forth in any of SEQ ID NOS: 125, 127, 224 and 226.

107. An isolated polypeptide, comprising at least one domain of a PDGFR-B as set forth in SEQ ID NO: 276, wherein the polypeptide lacks one or more amino acids of a transmembrane domain of the PDGFR-B, whereby the membrane localization of the polypeptide is reduced or abolished compared to the PDGFR-B.

108. The polypeptide of claim 107, that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the PDGFR-B.

109. The polypeptide of claim 107, wherein the polypeptide comprises at least one domain of PDGFR-B operatively linked to at least one amino acid encoded by an intron of a gene encoding the PDGFR-B.

110. The polypeptide of any of claims 107-109, wherein the polypeptide lacks one or more amino acids of a protein kinase domain of the PDGFR-B, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the PDGFR-B.

111. The polypeptide of any of claims 107-110, wherein the polypeptide comprises one or more amino acids of an immunoglobulin domain of the PDGFR-B.

112. The polypeptide of any of claims 107-111, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 147.

113. The polypeptide of any of claims 107-112, that comprises the amino acid sequence set forth in SEQ ID NO: 147 or an allelic variant thereof.

114. The polypeptide of claim 113, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 307.

115. The polypeptide of any of claims 107-114, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 147.

116. An isolated polypeptide, comprising at least one domain of a CSF1R as set forth in SEQ ID NO: 249, wherein the polypeptide lacks one ore more amino acids of a transmembrane domain of the CSF1R, whereby the membrane localization of the polypeptide is reduced or abolished compared to the CSF1R.

117. The polypeptide of claim 116, that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the CSF1R.

118. The polypeptide of claim 117, wherein the polypeptide comprises at least one domain of CSF1R operatively linked to at least one amino acid encoded by an intron of a gene encoding the CSF1R.

119. The polypeptide of any of claims 116-118, wherein the polypeptide lacks one or more amino acids of a protein kinase domain of the CSF1R, whereby the protein kinase activity of the polypeptide is reduced or abolished compared to the CSF1R.

120. The polypeptide of any of claims 116-119, wherein the polypeptide comprises one or more amino acids of an immunoglobulin domain of the CSF1R.

121. The polypeptide of any of claims 116-120, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 145.

122. The polypeptide of any of claims 116-121, that comprises the amino acid sequence set forth in SEQ ID NO: 145 or an allelic variant thereof.

123. The polypeptide of claim 122, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 285.

124. The polypeptide of any of claims 116-123, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 145.

125. An isolated polypeptide, comprising at least one domain of a KIT receptor as set forth in SEQ ID NO:273 and lacks one or more amino acids of a transmembrane domain and a protein kinase domain of the KIT receptor, whereby the membrane localization and protein kinase activity of the polypeptide are reduced or abolished compared to the KIT receptor.

126. The polypeptide of claim 125, that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the KIT receptor.

127. The polypeptide of claim 125, wherein the polypeptide comprises at least one domain of KIT receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding KIT receptor.

128. The polypeptide of any of claims 125-127, wherein the polypeptide comprises at least one immunoglobulin domain of the KIT receptor.

129. The polypeptide of any of claims 125-128, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 93.

130. The polypeptide of any of claims 125-129, that comprises the amino acid sequence set forth in SEQ ID NO: 93 or an allelic variant thereof.

131. The polypeptide of claim 130, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 305.

132. The polypeptide of any of claims 125-131, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 93.

133. An isolated polypeptide, comprising at least one cysteine rich c6 domain of a TNFR as set forth in SEQ ID NOS: 280 or 281 and lacks all of the transmembrane domain of the TNFR, whereby the membrane localization of the polypeptide is reduced or abolished compared to the TNFR.

134. The polypeptide of claim 133, that comprises an intron-encoded sequence of amino acids, wherein the intron is from a gene encoding the TNFR.

135. The polypeptide of claim 133, wherein the polypeptide comprises at least one domain of TNFR operatively linked to at least one amino acid encoded by an intron of a gene encoding the TNFR.

136. The polypeptide of any of claims 133-135, wherein the polypeptide comprises at least two cysteine rich c6 domains of the TNFR.

137. The polypeptide of any of claims 133-136, wherein the polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in SEQ ID NO: 95.

138. The polypeptide of any of claims 133-137, that comprises the amino acid sequence set forth in SEQ ID NO: 95 or an allelic variant thereof.

139. The polypeptide of claim 138, wherein the allelic variant comprises one or more amino acids of the allelic variations as set forth in SEQ ID NO: 312.

140. The polypeptide of any of claims 133-139, wherein the polypeptide contains the same number of amino acids as set forth in SEQ ID NO: 95.

141. The polypeptide of any of claims 1-140, wherein the polypeptide modulates a biological function of a cell surface receptor.

142. The polypeptide of claim 141, wherein the polypeptide modulates a biological function of the cognate receptor.

143. The polypeptide of claim 141 or claim 142, wherein the activity modulated by the polypeptide is one or more of: dimerization, homodimerization, heterodimerization, trimerization, kinase activity, receptor-associated kinase activity, receptor-associated protease activity, autophosphorylation of the cell surface receptor, transphosphorylation of the cell surface receptor, phosphorylation of a signal transduction molecule, ligand binding, competition with the cell surface receptor for ligand binding , signal transduction, interaction with a signal transduction molecule, induction of apoptosis, membrane association and membrane localization.

144. A pharmaceutical composition, comprising a polypeptide of any of claims 1-143.

145. The composition of claim 144, comprising an amount of the polypeptide effective for modulating an activity of a cell surface receptor.

146. The composition of claim 145, wherein the polypeptide modulates a biological function of the cognate receptor.

147. The composition of claim 145 or claim 146, wherein the activity modulated by the polypeptide is one or more of: dimerization, homodimerization, heterodimerization, trimerization, kinase activity, receptor-associated kinase activity, receptor-associated protease activity, autophosphorylation of the cell surface receptor, transphosphorylation of the cell surface receptor, phosphorylation of a signal transduction molecule, ligand binding, competition with the cell surface receptor for ligand binding , signal transduction, interaction with a signal transduction molecule, induction of apoptosis, membrane association and membrane localization.

148. The composition of any one of claims 145-147, wherein modulation is an inhibition of activity.

149. The composition of any one of claims 145-148, wherein the polypeptide of the composition complexes with a receptor tyrosine kinase or a tumor necrosis factor receptor.

150. A nucleic acid molecule, comprising a sequence of nucleic acids encoding a polypeptide of any of claims 1-143.

151. The nucleic acid molecule of claim 150, comprising an intron and an exon, wherein:

the intron contains a stop codon;

the nucleic acid molecule encodes an open reading frame that spans an exon intron junction; and

the open reading frame terminates at the stop codon in the intron.

152. The nucleic acid molecule of claim 151, wherein the intron encodes one or more amino acids of the encoded polypeptide.

153. The nucleic acid molecule of claim 151 or claim 152, wherein the stop codon is the first codon in the intron.

154. An isolated nucleic acid molecule, comprising the sequence of nucleic acids set forth in any of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126,

128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223 and 225 or an allelic variant thereof.

155. A vector, comprising the nucleic acid molecule of any of claims 150-154.

156. A cell, comprising the vector of claim 155.

157. A method of treating a disease or condition comprising, administering a pharmaceutical composition of any of claims 144-149.

158. The method of claim 157, wherein the disease or condition is selected from the group consisting of cancers, inflammatory diseases, infectious diseases angiogenesis-related conditions (conditions involving angiogenesis), cell proliferation-related conditions, conditions involving hyperproliferation of cells, immune disorders and neurodegenerative diseases.

159. The method of claim 157, wherein the disease or condition is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, posterior intraocular inflammation, uveitic disorders, ocular surface inflammatory disorders, neovascular disease, proliferative vitreoretinopathy, atherosclerosis, rheumatoid arthritis, hemangioma, diabetes mellitus, inflammatory bowel disease, psoriasis, Alzheimer's disease, lupus, vascular stenosis, restenosis, inflammatory joint disease, atherosclerosis, urinary obstructive syndromes, and asthma.

160. The method of claim 157, wherein the disease or condition is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, leukemia, lymphoid malignancies, squamous cell cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric cancer, stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney/renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, and head and neck cancer.

161. The method of claim 157, wherein the disease or condition includes infection by a virus or a parasite.

162. The method of claim 161, wherein the virus is selected from the group consisting of Myxoma virus, Vaccinia virus, Tanapox virus, Epstein-Barr virus, Herpes simplex virus, Cytomegalovirus, Herpesvirus saimiri, Hepatitis B virus, African swine fever virus, Parovirus, Human Immune deficiency virus (HIV), Hepatitis C virus, Influenza virus, Respiratory syncytial virus, Measles virus, Vesicular stomatitis virus, Dengue virus and Ebola virus.

163. The method of claim 157, wherein the pharmaceutical composition contains a polypeptide that inhibits angiogenesis, cell proliferation, cell migration, viral entry, viral infection, tumor cell growth or tumor cell metastasis.

164. An isolated polypeptide comprising the sequence of any one of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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 and 226.

165. An isolated polypeptide consisting essentially of the sequence of any one of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 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 and 226.

166. An isolated polypeptide, comprising a sequence of amino acids that has at least 80% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 or 155 or allelic variations thereof, wherein:

sequence identity is compared along the full length of each SEQ ID to the full length sequence of the isolated polypeptide;

each of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 and 155 is a cell surface receptor isoform.

167. An isolated polypeptide, comprising the sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 or 155.

168. The isolated polypeptide of claim 166, wherein the polypeptide contains the same number of amino acids as set forth in the SEQ ID to which it has identity.

169. The isolated polypeptide of claim 166, wherein the polypeptide occurs in a mammal.

170. The isolated polypeptide of claim 169, wherein the mammal is a rodent, a primate or a human.

171. An isolated polypeptide, comprising at least one domain of a cell surface receptor operatively linked to at least one amino acid encoded by an intron of a gene encoding the cell surface receptor;

wherein the cell surface receptor is selected from the group consisting of DDR1, KIT, FGFR-1, FGFR-4, TNFR2, VEGFR-1, VEGFR-3, RON, TEK, Tie-1, CSF1R, PDGFR-B, EphA1, and EphB1; or

wherein the polypeptide comprises a sequence of amino acids selected from the group consisting of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 and 155.

172. An isolated polypeptide, comprising a shortened cell surface receptor lacking at least all or part of a transmembrane domain, wherein:

the polypeptide is not membrane localized;

the polypeptide modulates an activity of the cell surface receptor;

the cell surface receptor is selected from the group consisting of DDR1, KIT, FGFR-1, FGFR-4, TNFR2, VEGFR-1, VEGFR-3, RON, TEK, Tie-1, CSF1R, PDGFR-B, EphA1, and EphB1, or the isolated polypeptide has at least 80% sequence identity with a sequence of amino acids set forth in any of SEQ ID NOS: 91, 93, 95, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153 or 155; and

sequence identity is compared along the full length of each SEQ ID to the sequence of the full length of the isolated polypeptide.

173. The isolated polypeptide of claim 172, wherein the cell surface receptor further lacks a cell surface receptor cytoplasmic domain.

174. An isolated polypeptide, comprising an intron-encoded sequence of amino acids, wherein:

the intron is from a cell surface receptor gene selected from the group consisting of KIT, FGFR-4, TNFR2, VEGFR-1, RON, TEK, Tie-1, and EphA1; or

the intron-encoded sequence of any of SEQ ID NOS: 91, 93, 95, 121, 123, 129, 131, 133, 135, 137, 139, 141, 149, 151 and 153; and

the polypeptide lacks a cell surface receptor cytoplasmic domain.

175. The polypeptide of claim 174, wherein the polypeptide further lacks a transmembrane domain.

176. The isolated polypeptide of claim 174 or claim 175, wherein the isolated polypeptide modulates a biological function of a cell surface receptor.

177. The isolated polypeptide of any of claims 166-176, wherein the polypeptide comprises a TNFR isoform and wherein the TNFR is selected from the group consisting of TNFR1, TNFR2, TNFRrp, the low-affinity nerve growth factor receptor, Fas antigen, CD40, CD27, CD30, 4-1BB, OX40, DR3, DR4, DR5, and herpesvirus entry mediator (HVEM).

178. A pharmaceutical composition, comprising a polypeptide of any of claims 171-177.

179. The composition of claim 178, comprising an amount of the polypeptide effective for modulating an activity of a cell surface receptor.

180. The composition of claim 179, wherein the activity of the cell surface receptor modulated by the polypeptide is one or more of dimerization, homodimerization, heterodimerization, trimerization, kinase activity, receptor-associated kinase activity, receptor-associated protease activity, autophosphorylation of the cell surface receptor, transphosphorylation of the cell surface receptor, phosphorylation of a signal transduction molecule, ligand binding, competition with the cell surface receptor for ligand binding , signal transduction, interaction with a signal transduction molecule, induction of apoptosis, membrane association and membrane localization.

181. The composition of claim 179 or claim 180, wherein modulation is an inhibition of activity.

182. The composition of claim 179 or claim 180, wherein the polypeptide of the composition complexes with a receptor tyrosine kinase or a tumor necrosis factor receptor.

183. A nucleic acid molecule encoding a polypeptide of any of claims 166-177.

184. The nucleic acid molecule of claim 183, comprising an intron and an exon, wherein:

the intron contains a stop codon;

the nucleic acid molecule encodes an open reading frame that spans an exon intron junction; and

the open reading frame terminates at the stop codon in the intron.

185. The nucleic acid molecule of claim 184, wherein the intron encodes one or more amino acids of the encoded polypeptide.

186. The nucleic acid molecule of claim 184 or claim 185, wherein the stop codon is the first codon in the intron.

187. An isolated nucleic acid molecule, comprising a sequence of nucleotides that has at least 90% sequence identity with a sequence of nucleotides set forth in any of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152 or 154 and allelic variations thereof, wherein:

sequence identity is compared along the full length of each SEQ ID to the full length sequence of the isolated nucleic acid molecule; and

each of SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152 and 154 is a cell surface receptor isoform.

188. An isolated nucleic acid molecule comprising SEQ ID NOS: 90, 92, 94, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152 or 154.

189. A vector, comprising the nucleic acid molecule of any of claims 183-188.

190. A cell, comprising the vector of claim 189.

191. A method of treating a disease or condition comprising, administering a pharmaceutical composition of any of claims 178-182.

192. The method of claim 191, wherein the disease or condition is selected from the group consisting of cancers, inflammatory diseases, infectious diseases, angiogenesis-related conditions, cell proliferation-related conditions, immune disorders and neurodegenerative diseases.

193. The method of claim 191, wherein the disease or condition is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, posterior intraocular inflammation, uveitic disorders, ocular surface inflammatory disorders, neovascular disease, proliferative vitreoretinopathy, atherosclerosis, rheumatoid arthritis, hemangioma, diabetes mellitus, inflammatory bowel disease, psoriasis, Alzheimer's disease, lupus, vascular stenosis, restenosis, inflammatory joint disease, atherosclerosis, urinary obstructive syndromes, and asthma.

194. The method of claim 191, wherein the disease or condition is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, leukemia, lymphoid malignancies, squamous cell cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric cancer, stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney/renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, and head and neck cancer.

195. The method of claim 191, wherein the disease or condition is infection by a virus or a parasite.

196. The method of claim 195, wherein the virus is selected from the group consisting of Myxoma virus, Vaccinia virus, Tanapox virus, Epstein-Barr virus, Herpes simplex virus, Cytomegalovirus, Herpesvirus saimiri, Hepatitis B virus,

African swine fever virus, Parovirus, Human Immune deficiency virus (HIV), Hepatitis C virus, Influenza virus, Respiratory syncytial virus, Measles virus, Vesicular stomatitis virus, Dengue virus and Ebola virus.

197. The method of claim 191, wherein the pharmaceutical composition contains a polypeptide that inhibits angiogenesis, cell proliferation, cell migration, viral entry, viral infection, tumor cell growth or tumor cell metastasis.

198. A method of regulating development and/or disease states, comprising contacting cells or tissues *in vitro* or *in vivo* with a cell surface receptor isoform (CSR) that lacks one or more domains or activities of the CSR, wherein the CSR is involved in angiogenesis or development

199. The method of claim 198, wherein the CSR is an intron fusion protein.

200. A chimeric polypeptide, comprising a portion of one cell surface receptor (CSR) isoform and a portion of a second, different CSR isoform, wherein:

the chimeric isoform modulates the activity of one or more tyrosine kinase receptors; and

each portion contains at least 4, 5, 6, 7, 8, 10, 12, 15, or more amino acid residues.

201. The polypeptide of claim 200, wherein the first and second cell surface receptor isoforms comprise a polypeptide selected from polypeptides of any of claims 1-143 and 165-177 or is a herstatin polypeptide.

202. The polypeptide of claim 200 or claim 201, wherein the first portion comprises all or part of an extracellular domain of a cell surface receptor; and the second portion comprises an intron from an intron fusion protein.

203. The polypeptide of claim 201, wherein the intron-encoded portion is a herstatin intron-encoded portion.

204. The polypeptide of claim 203, wherein the intron is set forth in any of SEQ ID NOS: 320-359.

205. A conjugate, comprising: a first portion linked directly or via a linker to an intron-encoded portion of an intron fusion polypeptide, wherein the resulting polypeptide modulates the activity of a cell surface receptor.

206. The conjugate of claim 205, wherein the first portion is all or part of an extracellular domain of any cell surface receptor (CSR).

207. The conjugate of claim 206, wherein the CSR is a receptor tyrosine kinase.

208. The conjugate of any of claims 205-207 or the chimeric polypeptides any of claims 200-204, wherein the first and second portions are from a polypeptide set forth in any of claims 1-143 and 164-177 or are from a herstatin, wherein if a portion is from herstatin the first or second portions are linked via a linker or on portion is not from a herstatin.

209. The conjugate or chimera of any of claims 200-207, wherein the first portion is from serum albumin.

210. The conjugate or chimera of any of claims 200-209, comprising an intron-encoded portion that is a herstatin intron.

211. A polypeptide comprising:

an N-terminal portion from a cell surface receptor other than HER-2 ; and an intron, wherein:

the polypeptide lacks at least all or part of a transmembrane domain; and

the polypeptide modulates the activity of a cell surface receptor.

212. The polypeptide of claim 211, wherein the CSR is an RTK.

213. A method of preparing a synthetic intron fusion protein, comprising:

linking the N-terminus of one cell surface receptor isoform to an intron from a intron fusion protein.

214. The method of claim 213, wherein the linkage is covalent.

215. The method of claim 213, wherein the linkage is peptidic.

216. The method of claim 213, wherein the CSR isoform is an intron fusion protein.

217. A pharmaceutical composition, comprising a polypeptide, chimeric polypeptide or conjugate of any of claims 200-212.

218. A method of treating a disease or condition comprising, administering a pharmaceutical composition of claim 217.

219. The method of claim 218, wherein the disease or condition is selected from the group consisting of cancers, inflammatory diseases, infectious diseases, angiogenesis-related conditions, cell proliferation-related conditions, immune disorders and neurodegenerative diseases.

220. The method of claim 218, wherein the disease or condition is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, posterior intraocular inflammation, uveitic disorders, ocular surface inflammatory disorders, neovascular disease, proliferative vitreoretinopathy, atherosclerosis, rheumatoid arthritis, hemangioma, diabetes mellitus, inflammatory bowel disease, psoriasis, Alzheimer's disease, lupus, vascular stenosis, restenosis, inflammatory joint disease, atherosclerosis, urinary obstructive syndromes, and asthma.

221. The method of claim 218, wherein the disease or condition is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, leukemia, lymphoid malignancies, squamous cell cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric cancer, stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney/renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, and head and neck cancer.

222. The method of claim 218, wherein the disease or condition is infection by a virus or a parasite.

223. The method of claim 222, wherein the virus is selected from the group consisting of Myxoma virus, Vaccinia virus, Tanapox virus, Epstein-Barr virus, Herpes simplex virus, Cytomegalovirus, Herpesvirus saimiri, Hepatitis B virus, African swine fever virus, Parovirus, Human Immune deficiency virus (HIV), Hepatitis C virus, Influenza virus, Respiratory syncytial virus, Measles virus, Vesicular stomatitis virus, Dengue virus and Ebola virus.

224. The method of claim 218, wherein the pharmaceutical composition contains a polypeptide that inhibits angiogenesis, cell proliferation, cell migration, viral entry, viral infection, tumor cell growth or tumor cell metastasis.

225. A method of regulating development and/or disease states, comprising contacting cells or tissues *in vitro* or *in vivo* with a polypeptide, chimeric polypeptide or conjugate of any of claims 1-143, 165-177, 200-212, thereby ameliorating the symptoms of the disease state or regulating development.

226. An isolated polypeptide, comprising at least one amino acid encoded by an intron of a gene encoding a polypeptide receptor isoform selected from among isoforms of FGFR-4, KIT, TNFRs, DDR1, FGFR-1, FGFR-4, VEGFR-2, VEGFR-3, RON, TEK, CSF1R, PDGFR-B, EphA, EphB, and MET.

227. The polypeptide of claim 226, wherein the polypeptide does not include a transmembrane domain.

228. The polypeptide of claim 226 or claim 227, that lacks at least one additional domain or a portion thereof whereby an activity is ablated or reduced or modified.

229. An isolated polypeptide of claim 226 that is a receptor antagonist.

230. A combination comprising:

two and one or more different cell surface receptor isoforms and/or a therapeutic drug or a cell surface receptor isoform and a therapeutic drug.

231. The combination of claim 230, wherein the isoforms and/or drugs are in separate compositions or in a single composition.

232. A method of treatment, comprising administering the components of the combination of claim 230, wherein each component is administered separately, simultaneously, intermittently, in a single composition or combinations thereof.

233. Use of a combination of claim 230 or claim 231 for the treatment of an angiogenic-related disorder, a tumor and/or an immune disorder.

234. Use of a combination of claim 230 or claim 231 for the formulation of a medicament for the treatment of angiogenic-related disorder, a tumor and/or an immune disorder.

SEQUENCE LISTING

<110> Jin, Pei
Shepard, H. Michael
Receptor Biologix Inc.

<120> CELL SURFACE RECEPTORS ISOFORMS AND METHODS OF IDENTIFYING AND USING SAME

<130> 17118-008WO1/2817PC

<140> Not yet assigned
<141> Herewith

<150> 60/571,289
<151> 2004-05-14

<150> 60/580,990
<151> 2004-06-18

<150> 60/666,825
<151> 2005-03-30

<160> 359

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 5084
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM_00022
<309> 2003-12-20

<400> 1
gatcccatcg cagctaccgc gatgagaggc gctcgcggcg cctgggattt tctctgcgtt 60
ctgctcctac tgcttcgcgt ccagacaggc tcttctcaac catctgtgag tccaggggaa 120
ccgtctccac catccatcca tccaggaaaa tcagacttaa tagtccgcgt gggcgacgag 180
attaggctgt tatgcactga tccgggcttt gtcaaatgga cttttgagat cctggatgaa 240
acgaatgaga ataagcagaa tgaatggatc acggaaaagg cagaagccac caacaccggc 300
aaatacacgt gcaccaacaa acacggctta agcaattcca tttatgtgtt tgttagagat 360
cctgccaagc ttttccttgt tgaccgctcc ttgtatggga aagaagacaa cgacacgctg 420
gtccgctgtc ctctcacaga cccagaagtg accaattatt ccctcaaggg gtgccagggg 480
aagcctcttc ccaaggactt gaggtttatt cctgacccca aggcgggcat catgatcaaa 540
agtgtgaaac gcgcctacca tcggctctgt ctgcattgtt ctgtggacca ggagggcaag 600
tcagtgctgt cggaaaaatt catcctgaaa gtgaggccag ccttcaaagc tgtgcctgtt 660
gtgtctgtgt ccaaagcaag ctatcttctt agggaagggg aagaattcac agtgacgtgc 720
acaataaaag atgtgtctag ttctgtgtac tcaacgtgga aaagagaaaa cagtcagact 780
aaactacagg agaaatataa tagctggcat cacggtgact tcaattatga acgtcaggca 840
acgttgacta tcagttcagc gagagttaat gattctggag tgttcatgtg ttatgccaat 900
aatacttttg gatcagcaaa tgtcacaaca accttggaag tagtagataa aggattcatt 960

aatatcttcc ccatgataaa cactacagta tttgtaaacg atggagaaaa tgtagatttg 1020
attgttgaat atgaagcatt ccccaaacct gaacaccagc agtggatcta tatgaacaga 1080
accttcactg ataaatggga agattatccc aagtctgaga atgaaagtaa tatcagatac 1140
gtaagtgaac ttcatctaac gagattaaaa ggcaccgaag gaggcactta cacattccta 1200
gtgtccaatt ctgacgtcaa tgctgccata gcatttaatg tttatgtgaa tacaaaacca 1260
gaaatcctga cttacgacag gctcgtgaat ggcatgctcc aatgtgtggc agcaggattc 1320
ccagagccca caatagattg gtatttttgt ccaggaactg agcagagatg ctctgcttct 1380
gtactgccag tggatgtgca gacactaaac tcatctgggc caccgtttgg aaagctagtg 1440
gttcagagtt ctatagattc tagtgcattc aagcacaatg gcacggttga atgtaaggct 1500
tacaacgatg tgggcaagac ttctgcctat tttaactttg catttaaagg taacaacaaa 1560
gagcaaatcc atccccacac cctgttcact cctttgctga ttggtttcgt aatcgtagct 1620
ggcatgatgt gcattattgt gatgattctg acctacaaat atttacagaa acccatgtat 1680
gaagtacagt ggaaggttgt tgaggagata aatggaaaca attatgttta catagaccca 1740
acacaacttc cttatgatca caaatgggag tttcccagaa acaggctgag ttttgggaaa 1800
accctgggtg ctggagcttt cgggaaggtt gttgaggcaa ctgcttatgg cttaattaag 1860
tcagatgcgg ccatgactgt cgctgtaaag atgctcaagc cgagtgccca tttgacagaa 1920
cgggaagccc tcatgtctga actcaaagtc ctgagttacc ttggtaatca catgaatatt 1980
gtgaatctac ttggagcctg caccattgga gggcccaccc tggtcattac agaatattgt 2040
tgctatggtg atcttttgaa ttttttgaga agaaaacgtg attcatttat ttgttcaaag 2100
caggaagatc atgcagaagc tgcactttat aagaatcttc tgcattcaaa ggagtcttcc 2160
tgcagcgata gtactaatga gtacatggac atgaaacctg gagtttctta tgttgtccca 2220
accaaggccg acaaaaggag atctgtgaga ataggctcat acatagaaag agatgtgact 2280
cccgccatca tggaggatga cgagttggcc ctagacttag aagacttgct gagcttttct 2340
taccaggtgg caaagggcat ggctttcctc gcctccaaga attgtattca cagagacttg 2400
gcagccagaa atatcctcct tactcatggt cggatcacaa agatttgtga ttttggtcta 2460
gccagagaca tcaagaatga ttctaattat gtggttaaag gaaacgctcg actacctgtg 2520
aagtggatgg cacctgaaag cattttcaac tgtgtataca cgtttgaaag tgacgtctgg 2580
tcctatggga tttttctttg ggagctgttc tctttaggaa gcagccccta tcctggaatg 2640
ccggtcgatt ctaagttcta caagatgatc aaggaaggct tccggatgct cagccctgaa 2700
cacgcacctg ctgaaatgta tgacataatg aagacttgct gggatgcaga tcccctaaaa 2760
agaccaacat tcaagcaaat tgttcagcta attgagaagc agatttcaga gagcaccaat 2820
catatttact ccaacttagc aaactgcagc cccaaccgac agaagcccgt ggtagaccat 2880
tctgtgcgga tcaattctgt cggcagcacc gcttcctcct cccagcctct gcttgtgcac 2940
gacgatgtct gagcagaatc agtgtttggg tcacccctcc aggaatgatc tcttcttttg 3000
gcttccatga tggttatttt cttttctttc aacttgcatc caactccagg atagtgggca 3060
ccccactgca atcctgtctt tctgagcaca ctttagtggc cgatgatttt tgtcatcagc 3120
caccatccta ttgcaaaggt tccaactgta tatattccca atagcaacgt agcttctacc 3180
atgaacagaa aacattctga tttggaaaaa gagagggagg tatggactgg gggccagagt 3240
cctttccaag gcttctccaa ttctgcccaa aaatatggtt gatagtttac ctgaataaat 3300
ggtagtaatc acagttggcc ttcagaacca tccatagtag tatgatgata caagattaga 3360
agctgaaaac ctaagtcctt tatgtggaaa acagaacatc attagaacaa aggacagagt 3420
atgaacacct gggcttaaga aatctagtat ttcatgctgg gaatgagaca taggccatga 3480
aaaaaatgat ccccaagtgt gaacaaaaga tgctcttctg tggaccactg catgagcttt 3540
tatactaccg acctggtttt taaatagagt ttgctattag agcattgaat tggagagaag 3600
gcctccctag ccagcacttg tatatacgca tctataaatt gtccgtgttc atacatttga 3660
ggggaaaaca ccataaggtt tcgtttctgt atacaaccct ggcattatgt ccactgtgta 3720
tagaagtaga ttaagagcca tataagtttg aaggaaacag ttaataccat tttttaagga 3780
aacaatataa ccacaaagca cagtttgaac aaaatctcct cttttagctg atgaacttat 3840
tctgtagatt ctgtggaaca agcctatcag cttcagaatg gcattgtact caatggattt 3900
gatgctgttt gacaaagtta ctgattcact gcatggctcc cacaggagtg ggaaaacact 3960
gccatcttag tttggattct tatgtagcag gaaataaagt ataggtttag cctccttcgc 4020
aggcatgtcc tggacaccgg gccagtatct atatatgtgt atgtacgttt gtatgtgtgt 4080
agacaaatat ttggaggggt atttttgccc tgagtccaag agggtccttt agtacctgaa 4140
aagtaacttg gctttcatta ttagtactgc tcttgtttct tttcacatag ctgtctagag 4200
tagcttacca gaagcttcca tagtggtgca gaggaagtgg aaggcatcag tccctatgta 4260
tttgcagttc acctgcactt aaggcactct gttatttaga ctcatcttac tgtacctgtt 4320

ccttagacct tccataatgc tactgtctca ctgaaacatt taaattttac cctttagact 4380
gtagcctgga tattattctt gtagtttacc tctttaaaaa caaaacaaaa caaaacaaaa 4440
aactcccctt cctcactgcc caatataaaa ggcaaatgtg tacatggcag agtttgtgtg 4500
ttgtcttgaa agattcaggt atgttgcctt tatggtttcc cccttctaca tttcttagac 4560
tacatttaga gaactgtggc cgttatctgg aagtaaccat ttgcactgga gttctatgct 4620
ctcgcacctt tccaaagtta acagattttg gggttgtgtt gtcacccaag agattgttgt 4680
ttgccatact ttgtctgaaa aattcctttg tgtttctatt gacttcaatg atagtaagaa 4740
aagtggttgt tagttataga tgtctaggta cttcaggggc acttcattga gagttttgtc 4800
ttgccatact ttgtctgaaa aattcctttg tgtttctatt gacttcaatg atagtaagaa 4860
aagtggttgt tagttataga tgtctaggta cttcaggggc acttcattga gagttttgtc 4920
aatgtctttt gaatattccc aagcccatga gtccttgaaa atatttttta tatatacagt 4980
aactttatgt gtaaatacat aagcggcgta agtttaaagg atgttggtgt tccacgtgtt 5040
ttattcctgt atgttgtcca attgttgaca gttctgaaga attc 5084

<210> 2
<211> 3015
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank NM_002011
<309> 2004-05-20

<400> 2
ccgaggagcg ctcgggctgt ctgcggaccc tgccgcgtgc aggggtcgcg gccggctgga 60
gctgggagtg aggcggcgga ggagccaggt gaggaggagc caggaaggca gttggtggga 120
agtccagctt gggtccctga gagctgtgag aaggagatgc ggctgctgct ggccctgttg 180
ggggtcctgc tgagtgtgcc tgggcctcca gtcttgtccc tggaggcctc tgaggaagtg 240
gagcttgagc cctgcctggc tcccagcctg gagcagcaag agcaggagct gacagtagcc 300
cttgggcagc ctgtgcggct gtgctgtggg cgggctgagc gtggtggcca ctggtacaag 360
gagggcagtc gcctggcacc tgctggccgt gtacggggct ggaggggccg cctagagatt 420
gccagcttcc tacctgagga tgctggccgc tacctctgcc tggcacgagg ctccatgatc 480
gtcctgcaga atctcacctt gattacaggt gactccttga cctccagcaa cgatgatgag 540
gaccccaagt cccataggga cctctcgaat aggcacagtt acccccagca agcaccctac 600
tggacacacc cccagcgcat ggagaagaaa ctgcatgcag tacctgcggg gaacaccgtc 660
aagttccgct gtccagctgc aggcaacccc acgcccacca tccgctggct taaggatgga 720
caggcctttc atggggagaa ccgcattgga ggcattcggc tgcgccatca gcactggagt 780
ctcgtgatgg agagcgtggt gccctcggac cgcggcacat acacctgcct ggtagagaac 840
gctgtgggca gcatccgcta taactacctg ctagatgtgc tggagcggtc cccgcaccgg 900
cccatcctgc aggccgggct cccggccaac accacagccg tggtgggcag cgacgtggag 960
ctgctgtgca aggtgtacag cgatgcccag ccccacatcc agtggctgaa gcacatcgtc 1020
atcaacggca gcagcttcgg agccgacggt ttcccctatg tgcaagtcct aaagactgca 1080
gacatcaata gctcagaggt ggaggtcctg tacctgcgga acgtgtcagc cgaggacgca 1140
ggcgagtaca cctgcctcgc aggcaattcc atcggcctct cctaccagtc tgcctggctc 1200
acggtgctgc cagaggagga ccccacatgg accgcagcag cgcccgaggc caggtatacg 1260
gacatcatcc tgtacgcgtc gggctccctg gccttggctg tgctcctgct gctggccggg 1320
ctgtatcgag ggcaggcgct ccacggccgg caccccccgcc cgcccgccac tgtgcagaag 1380
ctctcccgct tccctctggc ccgacagttc tccctggagt caggctcttc cggcaagtca 1440
agctcatccc tggtacgagg cgtgcgtctc tcctccagcg gccccgcctt gctcgccggc 1500
ctcgtgagtc tagatctacc tctcgaccca ctatgggagt tccccccggga caggctggtg 1560
cttgggaagc ccctaggcga gggctgcttt ggccaggtag tacgtgcaga ggcctttggc 1620
atggaccctg cccggcctga ccaagccagc actgtggccg tcaagatgct caaagacaac 1680
gcctctgaca aggacctggc cgacctggtc tcggagatgg aggtgatgaa gctgatcggc 1740
cgacacaaga acatcatcaa cctgcttggt gtctgcaccc aggaagggcc cctgtacgtg 1800
atcgtggagt gcgccgccaa gggaaacctg cgggagttcc tgcgggcccg gcgccccccca 1860

ggccccgacc tcagccccga cggtcctcgg agcagtgagg ggccgctctc cttcccagtc 1920
ctggtctcct gcgcctacca ggtggcccga ggcatgcagt atctggagtc ccggaagtgt 1980
atccaccggg acctggctgc ccgcaatgtg ctggtgactg aggacaatgt gatgaagatt 2040
gctgactttg ggctggcccg cggcgtccac cacattgact actataagaa aaccagcaac 2100
ggccgcctgc ctgtgaagtg gatggcgccc gaggccttgt ttgaccgggt gtacacacac 2160
cagagtgacg tgtggtcttt tgggatcctg ctatgggaga tcttcaccct cgggggctcc 2220
ccgtatcctg gcatcccggt ggaggagctg ttctcgctgc tgcgggaggg acatcggatg 2280
gaccgacccc cacactgccc cccagagctg tacgggctga tgcgtgagtg ctggcacgca 2340
gcgccctccc agaggcctac cttcaagcag ctggtggagg cgctggacaa ggtcctgctg 2400
gccgtctctg aggagtacct cgacctccgc ctgaccttcg gaccctattc cccctctggt 2460
ggggacgcca gcagcacctg ctcctccagc gattctgtct tcagccacga ccccctgcca 2520
ttgggatcca gctccttccc cttcgggtct ggggtgcaga catgagcaag gctcaaggct 2580
gtgcaggcac ataggctggt ggccttgggc cttggggctc agccacagcc tgacacagtg 2640
ctcgaccttg atagcatggg gcccctggcc cagagttgct gtgccgtgtc caagggccgt 2700
gcccttgccc ttggagctgc cgtgcctgtg tcctgatggc ccaaatgtca gggttctgct 2760
cggcttcttg gaccatggcg cttagtcccc atcccgggtt tggctgagcc tggctggaga 2820
gctgctatgc taaacctcct gcctcccaat accagcagga ggttctgggc ctctgaaccc 2880
cctttcccca cacctccccc tgctgctgct gccccagcgt cttgacggga gcattggccc 2940
ctgagcccag agaagctgga agcctgccga aaacaggagc aaatggcgtt ttataaatta 3000
ttttttttgaa ataaa 3015

<210> 3
<211> 3682
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank NM_001066
<309> 2003-12-20

<400> 3
gcgagcgcag cggagcctgg agagaaggcg ctgggctgcg agggcgcgag ggcgcgaggg 60
caggggggcaa ccggaccccg cccgcaccca tggcgcccgt cgccgtctgg gccgcgctgg 120
ccgtcggact ggagctctgg gctgcggcgc acgccttgcc cgcccaggtg gcatttacac 180
cctacgcccc ggagcccggg agcacatgcc ggctcagaga atactatgac cagacagctc 240
agatgtgctg cagcaaatgc tcgccgggcc aacatgcaaa agtcttctgt accaagacct 300
cggacaccgt gtgtgactcc tgtgaggaca gcacatacac ccagctctgg aactgggttc 360
ccgagtgctt gagctgtggc tcccgctgta gctctgacca ggtggaaact caagcctgca 420
ctcgggaaca gaaccgcatc tgcacctgca ggcccggctg gtactgcgcg ctgagcaagc 480
aggaggggtg ccggctgtgc gcgccgctgc gcaagtgccg cccgggcttc ggcgtggcca 540
gaccaggaac tgaaacatca gacgtggtgt gcaagccctg tgccccgggg acgttctcca 600
acacgacttc atccacggat atttgcaggc cccaccagat ctgtaacgtg gtggccatcc 660
ctgggaatgc aagcatggat gcagtctgca cgtccacgtc ccccacccgg agtatggccc 720
caggggcagt acacttaccc cagccagtgt ccacacgatc ccaacacacg cagccaactc 780
cagaacccag cactgctcca agcacctcct tcctgctccc aatgggcccc agccccccag 840
ctgaagggag cactggcgac ttcgctcttc cagttggact gattgtgggt gtgacagcct 900
tgggtctact aataatagga gtggtgaact gtgtcatcat gacccaggtg aaaaagaagc 960
ccttgtgcct gcagagagaa gccaaggtgc ctcacttgcc tgccgataag gcccggggta 1020
cacagggccc cgagcagcag cacctgctga tcacagcgcc gagctccagc agcagctccc 1080
tggagagctc ggccagtgcg ttggacagaa gggcgcccac tcggaaccag ccacaggcac 1140
caggcgtgga ggccagtggg gccggggagg cccgggccag caccgggagc tcagattctt 1200
cccctggtgg ccatgggacc caggtcaatg tcacctgcat cgtgaacgtc tgtagcagct 1260
ctgaccacag ctcacagtgc tcctcccaag ccagctccac aatgggagac acagattcca 1320
gcccctcgga gtccccgaag gacgagcagg tccccttctc caaggaggaa tgtgcctttc 1380
ggtcacagct ggagacgcca gagaccctgc tggggagcac cgaagagaag cccctgcccc 1440
ttggagtgcc tgatgctggg atgaagccca gttaaccagg ccggtgtggg ctgtgtcgta 1500

gccaaggtgg gctgagccct ggcaggatga ccctgcgaag gggccctggt ccttccaggc 1560
ccccaccact aggactctga ggctctttct gggccaagtt cctctagtgc cctccacagc 1620
cgcagcctcc ctctgacctg caggccaaga gcagaggcag cgagttgtgg aaagcctctg 1680
ctgccatggc gtgtccctct cggaaggctg gctgggcatg gacgttcggg gcatgctggg 1740
gcaagtccct gactctctgt gacctgcccc gcccagctgc acctgccagc ctggcttctg 1800
gagcccttgg gttttttgtt tgtttgtttg tttgtttgtt tgtttctccc cctgggctct 1860
gccccagctc tggcttccag aaaaccccag catccttttc tgcagagggg ctttctggag 1920
aggagggatg ctgcctgagt cacccatgaa gacaggacag tgcttcagcc tgaggctgag 1980
actgcgggat ggtcctgggg ctctgtgcag ggaggaggtg gcagccctgt agggaacggg 2040
gtccttcaag ttagctcagg aggcttggaa agcatcacct caggccaggt gcagtggctc 2100
acgcctatga tcccagcact ttgggaggct gaggcgggtg gatcacctga ggttaggagt 2160
tcgagaccag cctggccaac atggtaaaac cccatctcta ctaaaaatac agaaattagc 2220
cgggcgtggt ggcgggcacc tatagtccca gctactcaga agcctgaggc tgggaaatcg 2280
tttgaacccg ggaagcggag gttgcaggga gccgagatca cgccactgca ctccagcctg 2340
ggcgacagag cgagagtctg tctcaaaaga aaaaaaaaag caccgcctcc aaatgccaac 2400
ttgtcctttt gtaccatggt gtgaaagtca gatgcccaga gggcccaggc aggccaccat 2460
attcagtgct gtggcctggg caagataacg cacttctaac tagaaatctg ccaatttttt 2520
aaaaaagtaa gtaccactca ggccaacaag ccaacgacaa agccaaactc tgccagccac 2580
atccaacccc ccacctgcca tttgcaccct ccgccttcac tccggtgtgc ctgcagcccc 2640
gcgcctcctt ccttgctgtc ctaggccaca ccatctcctt tcagggaatt tcaggaacta 2700
gagatgactg agtcctcgta gccatctctc tactcctacc tcagcctaga ccctcctcct 2760
cccccagagg ggtgggttcc tcttccccac tccccacctt caattcctgg gccccaaacg 2820
ggctgccctg ccactttggt acatggccag tgtgatccca agtgccagtc ttgtgtctgc 2880
gtctgtgttg cgtgtcgtgg gtgtgtgtag ccaaggtcgg taagttgaat ggcctgcctt 2940
gaagccactg aagctgggat tcctccccat tagagtcagc cttccccctc ccagggccag 3000
ggccctgcag aggggaaacc agtgtagcct tgcccggatt ctgggaggaa gcaggttgag 3060
gggctcctgg aaaggctcag tctcaggagc atggggataa aggagaaggc atgaaattgt 3120
ctagcagagc aggggcaggg tgataaattg ttgataaatt ccactggact tgagcttggc 3180
agctgaacta ttggagggtg ggagagccca gccattacca tggagacaag aagggttttc 3240
caccctggaa tcaagatgtc agactggctg gctgcagtga cgtgcacctg tactcaggag 3300
gctgagggga ggatcactgg agcccaggag tttgaggctg cagcgagcta tgatcgcgcc 3360
actacactcc agcctgagca acagagtgag accctgtctc ttaaagaaaa aaaaagtcag 3420
actgctggga ctggccaggt ttctgcccac attggaccca catgaggaca tgatggagcg 3480
cacctgcccc ctggtggaca gtcctgggag aacctcaggc ttccttggca tcacagggca 3540
gagccgggaa gcgatgaatt tggagactct gtggggcctt ggttcccttg tgtgtgtgtg 3600
ttgatcccaa gacaatgaaa gtttgcactg tatgctggac ggcattcctg cttatcaata 3660
aacctgtttg ttttaaaaaa aa 3682

<210> 4
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer CSFIR_F1

<400> 4
ctgccacttc cccaccgagg 20

<210> 5
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR1_F1

<400> 5
gggatcagga gctatgggac ca 22

<210> 6
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR2_F1

<400> 6
ctgagatgat cctgattccc agaa 24

<210> 7
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA1_F1

<400> 7
ggagctatgg agcggcgctg 20

<210> 8
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA2_F1

<400> 8
agcgagaagc gcggcatgga 20

<210> 9
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA3_F1

<400> 9
caccagcaac atggattgtc agc 23

<210> 10
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA4_F1

<400> 10
cgaaccatgg ctgggatttt cta 23

<210> 11
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EOHA7_F1

<400> 11
ataaaacctg ctcatgcacc atg 23

<210> 12
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB1_F1

<400> 12
gcgatggccc tggattatct a 21

<210> 13
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB2_F1

<400> 13
ccccgggaag cgcagcca 18

<210> 14
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB3_F1

<400> 14
gctcctagag ctgccacggc 20

<210> 15
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB4_F1

<400> 15

gatcctaccc gagtgaggcg g 21

<210> 16
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer CSFIR_R1

<400> 16
gggctcctgc agagatgggt a 21

<210> 17
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR1_R1

<400> 17
agagccattg gggacacagg ga 22

<210> 18
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR2_R1

<400> 18
agcctgactc ctcctcccct g 21

<210> 19
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA1_R1

<400> 19
agctctgtca gcaagaccct gg 22

<210> 20
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA2_R1

<400> 20
aggtggtgtc tggggccagg tc 22

<210> 21
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA3_R1

<400> 21
gtcaggcttg aggctactga tgg 23

<210> 22
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA4_R1

<400> 22
aacataggaa gtgagagggt tcagg 25

<210> 23
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA7_R1

<400> 23
actccattgg gatgctctgg ttc 23

<210> 24
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB1_R1

<400> 24
agcccatcaa tccttgctgt g 21

<210> 25
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB2_R1

<400> 25
gcgtgcccgc acctggaaga 20

<210> 26
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB3_R1

<400> 26
gctggtcact gtggaggcga 20

<210> 27
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB4_R1

<400> 27
ggtagctggc tccccgcttc a 21

<210> 28
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer CSFIR_R2

<400> 28
ccgagggtct taccaaactg c 21

<210> 29
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR1_R2

<400> 29
aagcggagtc gagatcgagg ga 22

<210> 30
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer DDR2_R2

<400> 30
ggggaactcc tccacagcca 20

<210> 31

<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA1_R2

<400> 31
cgggtaaagt ccaaggctcc c 21

<210> 32
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA2_R2

<400> 32
gacacaggat ggatggatct cgg 23

<210> 33
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA3_R2

<400> 33
atcaatggat atgttggtgg catc 24

<210> 34
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA4_R2

<400> 34
aggatgcgtc aatttctttg gca 23

<210> 35
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA7_R2

<400> 35
ctgcaccaat cacacgctca a 21

<210> 36
<211> 22

<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB1_R2

<400> 36
atcaatctcc ttggcaaact cc 22

<210> 37
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB2_R2

<400> 37
gcccatgatg gaggcttcgc 20

<210> 38
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB3_R2

<400> 38
acgcaggaca cgtcgatctc c 21

<210> 39
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB4_R2

<400> 39
acctgcacca atcacctctt caa 23

<210> 40
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB6_F1

<400> 40
agagtggcgg gcatggtgtg 20

<210> 41
<211> 22
<212> DNA

<213> Artificial Sequence

<220>
<223> Primer EPHB6_R1

<400> 41
gcggagctga tagtccagga tg 22

<210> 42
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHB6_R2

<400> 42
cctgtcccaa tgacctcctc aa 22

<210> 43
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA6_F1

<400> 43
ggagatgaaa gactctccat ttcaag 26

<210> 44
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR1_F1

<400> 44
attcgggatg tggagctgga 20

<210> 45
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR2_F1

<400> 45
aggaccgggg attggtaccg 20

<210> 46
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR3_F1

<400> 46
catgggcgcc cctgcctg 18

<210> 47
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR4_F1

<400> 47
agaaggagat gcggctgctg 20

<210> 48
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TNFR1A(p55)_F1

<400> 48
agctgtctgg catgggcctc tc 22

<210> 49
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TNFR1B(p55)_F1

<400> 49
accggacccc gcccgcac 18

<210> 50
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer EPHA6_R1

<400> 50
atcttagacc gacagaaaat ttggc 25

<210> 51
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR1_R1

<400> 51
caagggacca tcctgcgtgc 20

<210> 52
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR2_R1

<400> 52
aggggcttgc ccagtgtcag 20

<210> 53
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR3_R1

<400> 53
gctcccattt ggggtcggca 20

<210> 54
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FGFR4_R1

<400> 54
cgggggaact cccatagtgg 20

<210> 55
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TNFR1A(p55)_R1

<400> 55
ggcgcagcct catctgagaa ga 22

<210> 56
<211> 20
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer TNFR1B(p55)_R1

<400> 56
cacagcccac accggcctgg 20

<210> 57
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FLT3_F1

<400> 57
ggaggccatg ccggcgttg 19

<210> 58
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer KIT_F1

<400> 58
cgcagctacc gcgatgagag g 21

<210> 59
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer MET_F1

<400> 59
ctcataatga aggcccccgc 20

<210> 60
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRA_F1

<400> 60
aagtttccca gagctatggg ga 22

<210> 61
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRB_F1

<400> 61
agcagcaagg acaccatgcg 20

<210> 62
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer RON_F1

<400> 62
ggtcccagct cgcctcgatg 20

<210> 63
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TEK_F1

<400> 63
agatttgggg aagcatggac tc 22

<210> 64
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TIE_F1

<400> 64
cggcctctgg agtatggtct g 21

<210> 65
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR1_F1

<400> 65
catggtcagc tactgggaca cc 22

<210> 66
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR2_F1

<400> 66
aggtgcagga tgcagagcaa g 21

<210> 67
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR3_F1

<400> 67
agcggccgga gatgcagcg 19

<210> 68
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FLT3_R1

<400> 68
ctgctcgaca cccactgtcc a 21

<210> 69
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer KIT_R1

<400> 69
gcagaagtct tgcccacatc g 21

<210> 70
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer MET_R1

<400> 70
cttcgtgatc ttcttcccag tga 23

<210> 71
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRA_R1

<400> 71

agattcttag ccaggcatcg ca 22

<210> 72
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRB_R1

<400> 72
agcgcaccga cagtggccga 20

<210> 73
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer RON_R1

<400> 73
gcacgggctg cccactgtca 20

<210> 74
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TEK_R1

<400> 74
ctgtccgagg ttccaaatag ttga 24

<210> 75
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TIE_R1

<400> 75
cgttctcact ggggtccacc a 21

<210> 76
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR1_R1

<400> 76
attattgcca tgcgctgagt ga 22

<210> 77
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR2_R1

<400> 77
gccgcttgga taacaagggt a 21

<210> 78
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR3_R1

<400> 78
aactcggtcc aggtgtccag gc 22

<210> 79
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer FLT3_R2

<400> 79
cttggaaact cccatttgag atca 24

<210> 80
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer KIT_R2

<400> 80
acaaccttcc cgaaagctcc a 21

<210> 81
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer MET_R2

<400> 81
actacatgct gcactgcctg ga 22

<210> 82
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRA_R2

<400> 82
cccgaccaag cactagtcca tc 22

<210> 83
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer PDGFRB_R2

<400> 83
ccagagccga gggtgcgtcc 20

<210> 84
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer RON_R2

<400> 84
caggtcattc aggttgggag ga 22

<210> 85
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TEK_R2

<400> 85
atttgatgtc attccagtca agca 24

<210> 86
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer TIE_R2

<400> 86
agcactgggt agctcagggg c 21

<210> 87

<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR1_R2

<400> 87
aactcccact tgctggcatc a 21

<210> 88
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR2_R2

<400> 88
aattcccatt tgctggcatc a 21

<210> 89
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer VEGFR3_R2

<400> 89
attcccactg gctggcatcg ta 22

<210> 90
<211> 713
<212> DNA
<213> Homo sapiens

<400> 90
tgggtccctg agagctgtga gaaggagatg cggctgctgc tggccctgtt gggggtcctg 60
ctgagtgtgc ctgggcctcc agtcttgtcc ctggaggcct ctgaggaagt ggagcttgca 120
agcattcatc tatcactgtg tctgcgagag aggactggcc ttgcagggcg cagggcccta 180
agctgggctg cagagctggt gagccctgcc tggctcccag cctggagcag caagagcagg 240
agctgacagt agcccttggg cagcctgtgc gtctgtgctg tgggcgggct gagcgtggtg 300
gccactggta caaggagggc agtcgcctgg cacctgctgg ccgtgtacgg ggctggaggg 360
gccgcctaga gattgccagc ttcctacctg aggatgctgg ccgctacctc tgcctggcac 420
gaggctccat gatcgtcctg cagaatctca ccttgattac aggtgactcc ttgacctcca 480
gcaacgatga tgaggacccc aagtcccata gggacccctc gaataggcac agttaccccc 540
agcaagcacc ctactggaca cacccccagc gcatggagaa gaaactgcat gcagtacctg 600
cggggaacac cgtcaagttc cgctgtccag ctgcaggcaa ccccacgccc accatccgct 660
ggcttaagga tggacaggcc tttcatgggg agaaccgcat tggaggcatt cgg 713

<210> 91
<211> 72
<212> PRT
<213> Homo sapiens

<400> 91
Met Arg Leu Leu Leu Ala Leu Leu Gly Val Leu Leu Ser Val Pro Gly
1 5 10 15
Pro Pro Val Leu Ser Leu Glu Ala Ser Glu Glu Val Glu Leu Ala Ser
20 25 30
Ile His Leu Ser Leu Cys Leu Arg Glu Arg Thr Gly Leu Ala Gly Arg
35 40 45
Arg Ala Leu Ser Trp Ala Ala Glu Leu Val Ser Pro Ala Trp Leu Pro
50 55 60
Ala Trp Ser Ser Lys Ser Arg Ser
65 70

<210> 92
<211> 1582
<212> DNA
<213> Homo sapiens

<400> 92
gatcccatcg cagctaccgc gatgagaggc gctcgcggcg cctgggattt tctctgcgtt 60
ctgctcctac tgcttcgcgt ccagacaggc tcttctcaac catctgtgag tccaggggaa 120
ccgtctccac catccatcca tccaggaaaa tcagacttaa tagtccgcgt gggcgacgag 180
attaggctgt tatgcactga tccgggcttt gtcaaatgga cttttgagat cctggatgaa 240
acgaatgaga ataagcagaa tgaatggatc acggaaaagg cagaagccac caacaccggc 300
aaatacacgt gcaccaacaa acacggctta agcaattcca tttatgtgtt tgttagagat 360
cctgccaagc ttttccttgt tgaccgctcc ttgtatggga aagaagacaa cgacacgctg 420
gtccgctgtc ctctcacaga cccagaagtg accaattatt ccctcaaggg gtgccagggg 480
aagcctcttc ccaaggactt gaggtttatt cctgacccca aggcgggcat catgatcaaa 540
agtgtgaaac gcgcctacca tcggctctgt ctgcattgtt ctgtggacca ggagggcaag 600
tcagtgctgt cggaaaaatt catcctgaaa gtgaggccag ccttcaaagc tgtgcctgtt 660
gtgtctgtgt ccaaagcaag ctatcttctt agggaagggg aagaattcac agtgacgtgc 720
acaataaaag atgtgtctag ttctgtgtac tcaacgtgga aaagagaaaa cagtcagact 780
aaactacagg agaaatataa tagctggcat cacggtgact tcaattatga acgtcaggca 840
acgttgacta tcagttcagc gagagttaat gattctggag tgttcatgtg ttatgccaat 900
aatacttttg gatcagcaaa tgtcacaaca accttggaag tagtagataa aggattcatt 960
aatatcttcc ccatgataaa cactacagta tttgtaaacg atggagaaaa tgtagatttg 1020
attgttgaat atgaagcatt ccccaaacct gaacaccagc agtggatcta tatgaacaga 1080
accttcactg ataaatggga agattatccc aagtctgaga atgaaagtaa tatcagatac 1140
gtaagtgaac ttcatctaac gagattaaaa ggcaccgaag gaggcactta cacattccta 1200
gtgtccaatt ctgacgtcaa tgctgccata gcatttaatg tttatgtgaa tacttccctg 1260
taaatagagt gattcggctt ttaatcggca ccacccttcc acccccaaaa aggagaaaat 1320
tcatcaaaac cagaaatcct gacttacgac aggctcgtga atggcatgct ccaatgtgtg 1380
gcagcaggat tcccagagcc cacaatagat tggtattttt gtccaggaac tgagcagaga 1440
tgctctgctt ctgtactgcc agtggatgtg cagacactaa actcatctgg gccaccgttt 1500
ggaaagctag tggttcagag ttctatagat tctagtgcat tcaagcacaa tggcacggtt 1560
gaatgtaagg cttacaacga tg 1582

<210> 93
<211> 413
<212> PRT
<213> Homo sapiens

<400> 93
Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
1 5 10 15
Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly

```
            20                  25                  30
Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
        35                  40                  45
Arg Val Gly Asp Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
    50                  55                  60
Lys Trp Thr Phe Glu Ile Leu Asp Glu Thr Asn Glu Asn Lys Gln Asn
65                  70                  75                  80
Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
                85                  90                  95
Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
            100                 105                 110
Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
        115                 120                 125
Asp Asn Asp Thr Leu Val Arg Cys Pro Leu Thr Asp Pro Glu Val Thr
    130                 135                 140
Asn Tyr Ser Leu Lys Gly Cys Gln Gly Lys Pro Leu Pro Lys Asp Leu
145                 150                 155                 160
Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
                165                 170                 175
Arg Ala Tyr His Arg Leu Cys Leu His Cys Ser Val Asp Gln Glu Gly
            180                 185                 190
Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
        195                 200                 205
Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg
    210                 215                 220
Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
225                 230                 235                 240
Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
                245                 250                 255
Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
            260                 265                 270
Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
        275                 280                 285
Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
    290                 295                 300
Leu Glu Val Val Asp Lys Gly Phe Ile Asn Ile Phe Pro Met Ile Asn
305                 310                 315                 320
Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
                325                 330                 335
Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
            340                 345                 350
Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
        355                 360                 365
Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
    370                 375                 380
Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385                 390                 395                 400
Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Ser Leu
                405                 410
```

<210> 94
<211> 913
<212> DNA
<213> Homo sapiens

<400> 94
agaaggcgct gggctgcgag ggcgcgaggg cgcgagggca gggggcaacc ggaccccgcc 60
cgcacccatg gcgcccgtcg ccgtctgggc cgcgctggcc gtcggactgg agctctgggc 120
tgcggcgcac gccttgcccg cccaggtggc atttacaccc tacgccccgg agcccgggag 180
cacatgccgg ctcagagaat actatgacca gacagctcag atgtgctgca gcaaatgctc 240
gccgggccaa catgcaaaag tcttctgtac caagacctcg gacaccgtgt gtgactcctg 300
tgaggacagc acatacaccc agctctggaa ctgggttccc gagtgcttga gctgtggctc 360
ccgctgtagc tctgaccagg tggaaactca agcctgcact cgggaacaga accgcatctg 420
cacctgcagg cccggctggt actgcgcgct gagcaagcag gaggggtgcc ggctgtgcgc 480
gccgctgcgc aagtgccgcc cgggcttcgg cgtggccaga ccagacctct cctagggctc 540
tagtgccaag gcccagctgt cccgcagagt gtctgagtgg ttgacaagtt cggattgttc 600
cctgaaggaa ctgaaacatc agacgtggtg tgcaagccct gtgccccggg gacgttctcc 660
aacacgactt catccacgga tatttgcagg ccccaccaga tctgtaacgt ggtggccatc 720
cctgggaatg caagcatgga tgcagtctgc acgtccacgt cccccacccg gagtatggcc 780
ccaggggcag tacacttacc ccagccagtg tccacacgat cccaacacac gcagccaact 840
ccagaaccca gcactgctcc aagcacctcc ttcctgctcc caatgggccc cagcccccca 900
gctgaaggga gca 913

<210> 95
<211> 155
<212> PRT
<213> Homo sapiens

<400> 95
Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15
Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
20 25 30
Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
35 40 45
Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
50 55 60
Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65 70 75 80
Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
85 90 95
Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
100 105 110
Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
115 120 125
Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
130 135 140
Pro Gly Phe Gly Val Ala Arg Pro Asp Leu Ser
145 150 155

<210> 96
<211> 680
<212> PRT
<213> Homo sapiens

<400> 96
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp
20 25 30

```
Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu
        35                  40                  45
Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu
    50                  55                  60
Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln
65                  70                  75                  80
Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val
                85                  90                  95
Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp
            100                 105                 110
Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr
        115                 120                 125
Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu
    130                 135                 140
Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn
145                 150                 155                 160
Pro Gln Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His
                165                 170                 175
Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg
            180                 185                 190
Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly
        195                 200                 205
Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly
    210                 215                 220
Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu
225                 230                 235                 240
Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala
                245                 250                 255
Cys Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala
            260                 265                 270
Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu
        275                 280                 285
Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn
    290                 295                 300
Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His
305                 310                 315                 320
Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys
                325                 330                 335
Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu
            340                 345                 350
Arg Glu Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly
        355                 360                 365
Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp
    370                 375                 380
Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln
385                 390                 395                 400
Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala
                405                 410                 415
Trp Pro Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val
            420                 425                 430
Ile Arg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln
        435                 440                 445
Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly
    450                 455                 460
Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His
465                 470                 475                 480
```

```
Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu
                485                 490                 495
His Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala
            500                 505                 510
Cys His Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr
        515                 520                 525
Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu
    530                 535                 540
Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg
545                 550                 555                 560
His Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val
                565                 570                 575
Thr Cys Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr
            580                 585                 590
Lys Asp Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro
        595                 600                 605
Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala
    610                 615                 620
Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp
625                 630                 635                 640
Asp Lys Gly Cys Pro Ala Glu Gln Arg Ala Arg Leu Ala Trp Thr Pro
                645                 650                 655
Gly Cys Thr Leu His Cys Pro Ser Leu Pro His Trp Met Leu Gly Gly
            660                 665                 670
His Cys Cys Arg Glu Gly Thr Pro
        675                 680
```

<210> 97
<211> 633
<212> PRT
<213> Homo sapiens

<400> 97

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
```

```
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
        435                 440                 445
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460
Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495
Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
            500                 505                 510
Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
        515                 520                 525
Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
    530                 535                 540
Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
                565                 570                 575
Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
            580                 585                 590
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605
Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620
```

Pro Cys Pro Ile Asn Cys Thr His Ser
625 630

<210> 98
<211> 575
<212> PRT
<213> Homo sapiens

<400> 98
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340 345 350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355 360 365

```
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
        435                 440                 445
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460
Leu Ala Leu Ile His His Tyr Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495
Ala Asn Arg Pro Glu Asp Glu Cys Gly Lys Thr Gly Ser Pro Val Cys
            500                 505                 510
Ala Leu Pro Ile Cys Gln His Thr Ala Val Pro Arg Gly Pro Trp Gln
        515                 520                 525
Gln Arg Ser Trp Thr Cys Ala Asp Cys Pro Ser Leu Cys Thr Leu Leu
    530                 535                 540
Asp Ser Ala Gln Leu Trp Leu Ala Trp Pro Leu Gly Met Ala Ser Leu
545                 550                 555                 560
Ala Gly Ser Tyr Leu Pro Trp His Pro Ser Leu Pro Leu Cys Phe
                565                 570                 575
```

<210> 99
<211> 523
<212> PRT
<213> Homo sapiens

<400> 99

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
```

```
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350
Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365
Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380
Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400
Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415
Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430
Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile Lys Trp
        435                 440                 445
Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys Asp Phe
    450                 455                 460
Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser Asn Met
465                 470                 475                 480
Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile Glu Gly
                485                 490                 495
Lys Asn Lys Leu Pro Pro Ala Asn Ser Ser Phe Met Leu Pro Pro Thr
            500                 505                 510
Ser Phe Ser Ser Asn Tyr Phe His Phe Leu Pro
        515                 520


<210> 100
<211> 541
<212> PRT
<213> Homo sapiens

<400> 100
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
```

```
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350
Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365
Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380
Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400
Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415
Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430
Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445
Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460
Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465                 470                 475                 480
```

```
Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495
Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510
Glu Gly Lys Asn Lys Leu Pro Pro Ala Asn Ser Ser Phe Met Leu Pro
        515                 520                 525
Pro Thr Ser Phe Ser Ser Asn Tyr Phe His Phe Leu Pro
    530                 535                 540
```

<210> 101
<211> 436
<212> PRT
<213> Homo sapiens

<400> 101

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
```

```
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350
Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365
Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380
Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Lys Asn Leu Thr Ala Thr
385                 390                 395                 400
Leu Ile Val Asn Val Lys Pro Gln Glu Arg Ile Arg Glu Arg Ile Ser
                405                 410                 415
Pro Asp Leu Tyr Arg Ile Trp Tyr Pro Ser Thr Tyr Asn Gln Val Val
            420                 425                 430
Leu Ala Pro Leu
        435
```

<210> 102
<211> 365
<212> PRT
<213> Homo sapiens

<400> 102

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
```

```
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
Ser Val Asn Thr Ser Val His Ile Tyr Gly Lys His Ser Ser Ala Leu
                325                 330                 335
Pro Thr His Ala Met Leu Ser Asn His Cys Arg Cys Leu Cys Ser Leu
            340                 345                 350
Asn Lys Ser Val Phe Cys Trp Pro Arg Val Thr Leu Ser
        355                 360                 365


<210> 103
<211> 934
<212> PRT
<213> Homo sapiens

<400> 103
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1               5                  10                  15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35                  40                  45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
```

```
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720
```

```
Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780
Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800
Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815
Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830
Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845
Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
    850                 855                 860
Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865                 870                 875                 880
Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
                885                 890                 895
Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Val Gly
            900                 905                 910
Phe Leu His Ser Ser His Asp Val Asn Lys Glu Ala Ser Val Ile Met
        915                 920                 925
Leu Phe Ser Gly Leu Lys
    930
```

<210> 104
<211> 821
<212> PRT
<213> Homo sapiens

<400> 104

```
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
```

```
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Gly Ile Gln Arg
    290                 295                 300
Met Thr Pro Lys Ile Val Asp Leu Pro Asp His Ile Glu Val Asn Ser
305                 310                 315                 320
Gly Lys Phe Asn Pro Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr
                325                 330                 335
Asn Glu Glu Met Thr Leu Val Lys Pro Asp Gly Thr Val Leu His Pro
            340                 345                 350
Lys Asp Phe Asn His Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile
        355                 360                 365
His Arg Ile Leu Pro Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn
    370                 375                 380
Thr Val Ala Gly Met Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val
385                 390                 395                 400
Leu Pro Lys Pro Leu Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn
                405                 410                 415
Phe Ala Val Ile Asn Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro
            420                 425                 430
Ile Lys Ser Lys Lys Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala
        435                 440                 445
Trp Gln His Ile Gln Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu
    450                 455                 460
Glu Pro Arg Thr Glu Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly
465                 470                 475                 480
Glu Gly Gly Glu Gly His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala
                485                 490                 495
Ser Ile Gly Leu Pro Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser
            500                 505                 510
Gln Thr Thr Leu Asn Leu Thr Trp Gln Pro Ser Ser Glu Asp Asp Phe
        515                 520                 525
Tyr Val Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn
    530                 535                 540
Ile Lys Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His
545                 550                 555                 560
Pro Arg Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln
                565                 570                 575
Gly Glu Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu
            580                 585                 590
Pro Pro Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser
        595                 600                 605
```

```
Ala Val Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile
    610                 615                 620
Thr Ile Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp
625                 630                 635                 640
Val Lys Ile Lys Asn Ala Thr Ile Thr Gln Tyr Gln Leu Lys Gly Leu
                645                 650                 655
Glu Pro Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile
            660                 665                 670
Gly Ser Ser Asn Pro Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu
        675                 680                 685
Ser Gln Ala Pro Ala Asp Leu Gly Gly Gly Lys Met Leu Leu Ile Ala
    690                 695                 700
Ile Leu Gly Ser Ala Gly Met Thr Cys Leu Thr Val Leu Leu Ala Phe
705                 710                 715                 720
Leu Ile Ile Leu Gln Leu Lys Arg Ala Asn Val Gln Arg Arg Met Ala
                725                 730                 735
Gln Ala Phe Gln Asn Val Arg Glu Glu Pro Ala Val Gln Phe Asn Ser
            740                 745                 750
Gly Thr Leu Ala Leu Asn Arg Lys Val Lys Asn Asn Pro Asp Pro Thr
        755                 760                 765
Ile Tyr Pro Val Leu Asp Trp Asn Asp Ile Lys Phe Gln Asp Val Ile
    770                 775                 780
Gly Glu Gly Asn Phe Gly Gln Val Leu Lys Ala Arg Ile Lys Lys Asp
785                 790                 795                 800
Gly Leu Arg Met Asp Ala Ala Ile Lys Arg Met Lys Glu Tyr Ala Ser
                805                 810                 815
Lys Asp Asp His Arg
            820
```

<210> 105
<211> 864
<212> PRT
<213> Homo sapiens

<400> 105

```
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
```

```
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
    290                 295                 300
Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305                 310                 315                 320
Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
                325                 330                 335
Gly Leu Gln Cys Glu Arg Glu Gly Ile Gln Arg Met Thr Pro Lys Ile
            340                 345                 350
Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
        355                 360                 365
Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
    370                 375                 380
Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
385                 390                 395                 400
Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
                405                 410                 415
Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
            420                 425                 430
Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
        435                 440                 445
Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
    450                 455                 460
Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
465                 470                 475                 480
Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
                485                 490                 495
Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
            500                 505                 510
Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly
        515                 520                 525
His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro
    530                 535                 540
Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn
545                 550                 555                 560
Leu Thr Trp Gln Pro Ser Ser Glu Asp Asp Phe Tyr Val Glu Val Glu
                565                 570                 575
Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys Val Pro Gly
            580                 585                 590
Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg Glu Gln Tyr
        595                 600                 605
```

```
Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu Trp Ser Glu
    610                 615                 620
Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro Gln Pro Glu
625                 630                 635                 640
Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val Ile Ser Trp
                645                 650                 655
Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile Arg Tyr Lys
            660                 665                 670
Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys Ile Lys Asn
        675                 680                 685
Ala Thr Ile Thr Gln Tyr Gln Leu Lys Gly Leu Glu Pro Glu Thr Ala
    690                 695                 700
Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser Ser Asn Pro
705                 710                 715                 720
Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln Ala Pro Ala
                725                 730                 735
Asp Leu Gly Gly Gly Lys Met Leu Leu Ile Ala Ile Leu Gly Ser Ala
            740                 745                 750
Gly Met Thr Cys Leu Thr Val Leu Leu Ala Phe Leu Ile Ile Leu Gln
        755                 760                 765
Leu Lys Arg Ala Asn Val Gln Arg Arg Met Ala Gln Ala Phe Gln Asn
    770                 775                 780
Val Arg Glu Glu Pro Ala Val Gln Phe Asn Ser Gly Thr Leu Ala Leu
785                 790                 795                 800
Asn Arg Lys Val Lys Asn Asn Pro Asp Pro Thr Ile Tyr Pro Val Leu
                805                 810                 815
Asp Trp Asn Asp Ile Lys Phe Gln Asp Val Ile Gly Glu Gly Asn Phe
            820                 825                 830
Gly Gln Val Leu Lys Ala Arg Ile Lys Lys Asp Gly Leu Arg Met Asp
        835                 840                 845
Ala Ala Ile Lys Arg Met Lys Glu Tyr Ala Ser Lys Asp Asp His Arg
    850                 855                 860


<210> 106
<211> 444
<212> PRT
<213> Homo sapiens

<400> 106
Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
 1               5                  10                  15
Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
            20                  25                  30
Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
        35                  40                  45
Ala Ser Ser Ser Trp Ser Asp Ser Thr Ala Ala Arg His Ser Arg Leu
    50                  55                  60
Glu Ser Ser Asp Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65                  70                  75                  80
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
                85                  90                  95
Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys
            100                 105                 110
Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
        115                 120                 125
```

```
Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
    130                 135                 140
Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145                 150                 155                 160
Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Val Met Ser Val
                165                 170                 175
Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu
            180                 185                 190
Ser Tyr Thr Ala Pro Val Gly Gln Thr Met Tyr Leu Ser Glu Ala Val
        195                 200                 205
Tyr Leu Asn Asp Ser Thr Tyr Asp Gly His Thr Val Gly Gly Leu Gln
    210                 215                 220
Tyr Gly Gly Leu Gly Gln Leu Ala Asp Gly Val Val Gly Leu Asp Asp
225                 230                 235                 240
Phe Arg Lys Ser Gln Glu Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val
                245                 250                 255
Gly Trp Ser Asn His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe
            260                 265                 270
Glu Phe Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Val His Cys Asn
        275                 280                 285
Asn Met His Thr Leu Gly Ala Arg Leu Pro Gly Gly Val Glu Cys Arg
    290                 295                 300
Phe Arg Arg Gly Pro Ala Met Ala Trp Glu Gly Glu Pro Met Arg His
305                 310                 315                 320
Asn Leu Gly Gly Asn Leu Gly Asp Pro Arg Ala Arg Ala Val Ser Val
                325                 330                 335
Pro Leu Gly Gly Arg Val Ala Arg Phe Leu Gln Cys Arg Phe Cys Pro
            340                 345                 350
His Leu Pro Arg Thr Ala Ser Pro Ile Met Pro Arg Leu Thr Leu Leu
        355                 360                 365
Pro Cys Arg Ala Ser Pro Gly Ala Thr Pro Met Leu Cys Leu His Cys
    370                 375                 380
Pro Gln Gly Gln Ser Gly Met Gly Pro Pro Glu Trp Ile Ser Leu Asp
385                 390                 395                 400
Leu Asp Ser Ala Ser Arg Arg Ser Leu Ala Arg Ala Ser Leu Gly Arg
                405                 410                 415
Cys Thr Cys Val Arg Ser Thr Ala Leu Lys Ile Trp Leu Val Leu Ile
            420                 425                 430
Ser Pro Leu Met Cys Val Arg Asp Thr Leu Cys Trp
        435                 440


<210> 107
<211> 166
<212> PRT
<213> Homo sapiens

<400> 107
Met Asp Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro
 1               5                  10                  15
Pro Lys Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro
            20                  25                  30
Leu Tyr Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp
        35                  40                  45
His Trp Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg
    50                  55                  60
```

```
Val His Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro
65                  70                  75                  80
Gly Gly Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr
                85                  90                  95
Met Glu Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe
            100                 105                 110
Gln Lys Val Leu Leu Pro Ser Met Pro Ser Gly Ser Trp Cys Arg Ser
        115                 120                 125
Leu Val Ala Pro Tyr Trp Val Pro Glu Lys Val Ala Glu Thr Gly Arg
    130                 135                 140
Gly Cys Arg Gly Arg Ile Leu Lys Arg Ile Trp Arg Leu Lys Ala Gly
145                 150                 155                 160
His Gly Gly Leu Cys Leu
                165
```

<210> 108
<211> 90
<212> PRT
<213> Homo sapiens

<400> 108

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Val Arg Pro Val Gly
65                  70                  75                  80
Asn Pro Ala Arg Pro Cys Leu Gln Leu Gly
                85                  90
```

<210> 109
<211> 209
<212> PRT
<213> Homo sapiens

<400> 109

```
Met Met Arg Thr Pro Ser Pro Ile Gly Thr Pro Arg Ile Gly Thr Val
 1               5                  10                  15
Thr Pro Ser Lys Val Ser Arg Ser Pro Arg Thr Cys Val Pro Ala Ala
            20                  25                  30
Ala His Leu Ile Thr Glu Lys Arg Arg Pro Val Trp Glu His Thr Val
        35                  40                  45
Ile Leu Gly Ala Phe Pro Cys Pro Pro Ala Pro Tyr Trp Thr His Pro
    50                  55                  60
Gln Arg Met Glu Lys Lys Leu His Ala Val Pro Ala Gly Asn Thr Val
65                  70                  75                  80
Lys Phe Arg Cys Pro Ala Ala Gly Asn Pro Thr Pro Thr Ile Arg Trp
                85                  90                  95
Leu Lys Asp Gly Gln Ala Phe His Gly Glu Asn Arg Ile Gly Gly Ile
            100                 105                 110
```

```
Arg Leu Arg His Gln His Trp Ser Leu Val Met Glu Ser Val Val Pro
        115                 120                 125
Ser Asp Arg Gly Thr Tyr Thr Cys Leu Val Glu Asn Ala Val Gly Ser
    130                 135                 140
Ile Arg Tyr Asn Tyr Leu Leu Asp Val Leu Glu Arg Ser Pro His Arg
145                 150                 155                 160
Pro Ile Leu Gln Ala Gly Leu Pro Ala Asn Thr Thr Ala Val Val Gly
                165                 170                 175
Ser Asp Val Glu Leu Leu Cys Lys Val Tyr Ser Asp Ala Gln Pro His
            180                 185                 190
Ile Gln Trp Leu Lys His Ile Val Ile Asn Gly Ser Ser Phe Gly Ala
        195                 200                 205
Asp
```

<210> 110
<211> 479
<212> PRT
<213> Homo sapiens

<400> 110

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
```

```
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350
Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365
Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380
Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400
Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415
Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430
Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445
Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460
Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg
465                 470                 475
```

<210> 111
<211> 217
<212> PRT
<213> Homo sapiens

<400> 111

```
Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
 1               5                  10                  15
Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
            20                  25                  30
Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
        35                  40                  45
Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
    50                  55                  60
Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65                  70                  75                  80
Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
                85                  90                  95
Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
            100                 105                 110
Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
        115                 120                 125
Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
    130                 135                 140
Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145                 150                 155                 160
Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
                165                 170                 175
```

```
Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
            180                 185                 190
Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
        195                 200                 205
Lys Gly Thr Cys Ile Ile Ser Phe Leu
    210                 215
```

<210> 112
<211> 798
<212> PRT
<213> Homo sapiens

<400> 112

```
Met Asp Leu Ile Leu Ile Asn Ser Leu Pro Leu Val Ser Asp Ala Glu
 1               5                  10                  15
Thr Ser Leu Thr Cys Ile Ala Ser Gly Trp Arg Pro His Glu Pro Ile
            20                  25                  30
Thr Ile Gly Arg Asp Phe Glu Ala Leu Met Asn Gln His Gln Asp Pro
        35                  40                  45
Leu Glu Val Thr Gln Asp Val Thr Arg Glu Trp Ala Lys Lys Val Val
    50                  55                  60
Trp Lys Arg Glu Lys Ala Ser Lys Ile Asn Gly Ala Tyr Phe Cys Glu
65                  70                  75                  80
Gly Arg Val Arg Gly Glu Ala Ile Arg Ile Arg Thr Met Lys Met Arg
                85                  90                  95
Gln Gln Ala Ser Phe Leu Pro Ala Thr Leu Thr Met Thr Val Asp Lys
            100                 105                 110
Gly Asp Asn Val Asn Ile Ser Phe Lys Lys Val Leu Ile Lys Glu Glu
        115                 120                 125
Asp Ala Val Ile Tyr Lys Asn Gly Ser Phe Ile His Ser Val Pro Arg
    130                 135                 140
His Glu Val Pro Asp Ile Leu Glu Val His Leu Pro His Ala Gln Pro
145                 150                 155                 160
Gln Asp Ala Gly Val Tyr Ser Ala Arg Tyr Ile Gly Gly Asn Leu Phe
                165                 170                 175
Thr Ser Ala Phe Thr Arg Leu Ile Val Arg Arg Cys Glu Ala Gln Lys
            180                 185                 190
Trp Gly Pro Glu Cys Asn His Leu Cys Thr Ala Cys Met Asn Asn Gly
        195                 200                 205
Val Cys His Glu Asp Thr Gly Glu Cys Ile Cys Pro Pro Gly Phe Met
    210                 215                 220
Gly Arg Thr Cys Glu Lys Ala Cys Glu Leu His Thr Phe Gly Arg Thr
225                 230                 235                 240
Cys Lys Glu Arg Cys Ser Gly Gln Glu Gly Cys Lys Ser Tyr Val Phe
                245                 250                 255
Cys Leu Pro Asp Pro Tyr Gly Cys Ser Cys Ala Thr Gly Trp Lys Gly
            260                 265                 270
Leu Gln Cys Asn Glu Gly Ile Gln Arg Met Thr Pro Lys Ile Val Asp
        275                 280                 285
Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro Ile Cys
    290                 295                 300
Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr Leu Val
305                 310                 315                 320
Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His Thr Asp
                325                 330                 335
```

```
His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro Pro Asp
            340                 345                 350
Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met Val Glu
        355                 360                 365
Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu Asn Ala
    370                 375                 380
Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn Ile Ser
385                 390                 395                 400
Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys Leu Leu
                405                 410                 415
Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln Val Thr
            420                 425                 430
Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu Tyr Glu
        435                 440                 445
Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly His Pro
    450                 455                 460
Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro Pro Pro
465                 470                 475                 480
Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn Leu Thr
                485                 490                 495
Trp Gln Pro Ser Ser Glu Asp Asp Phe Tyr Val Glu Val Glu Arg Arg
            500                 505                 510
Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys Val Pro Gly Asn Leu
        515                 520                 525
Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg Glu Gln Tyr Val Val
    530                 535                 540
Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu Trp Ser Glu Asp Leu
545                 550                 555                 560
Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro Gln Pro Glu Asn Ile
                565                 570                 575
Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val Ile Ser Trp Thr Ile
            580                 585                 590
Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile Arg Tyr Lys Val Gln
        595                 600                 605
Gly Lys Asn Glu Asp Gln His Val Asp Val Lys Ile Lys Asn Ala Thr
    610                 615                 620
Ile Thr Gln Tyr Gln Leu Lys Gly Leu Glu Pro Glu Thr Ala Tyr Gln
625                 630                 635                 640
Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser Ser Asn Pro Ala Phe
                645                 650                 655
Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln Ala Pro Ala Asp Leu
            660                 665                 670
Gly Gly Gly Lys Met Leu Leu Ile Ala Ile Leu Gly Ser Ala Gly Met
        675                 680                 685
Thr Cys Leu Thr Val Leu Leu Ala Phe Leu Ile Ile Leu Gln Leu Lys
    690                 695                 700
Arg Ala Asn Val Gln Arg Arg Met Ala Gln Ala Phe Gln Asn Val Arg
705                 710                 715                 720
Glu Glu Pro Ala Val Gln Phe Asn Ser Gly Thr Leu Ala Leu Asn Arg
                725                 730                 735
Lys Val Lys Asn Asn Pro Asp Pro Thr Ile Tyr Pro Val Leu Asp Trp
            740                 745                 750
Asn Asp Ile Lys Phe Gln Asp Val Ile Gly Glu Gly Asn Phe Gly Gln
        755                 760                 765
Val Leu Lys Ala Arg Ile Lys Lys Asp Gly Leu Arg Met Asp Ala Ala
    770                 775                 780
```

```
Ile Lys Arg Met Lys Glu Tyr Ala Ser Lys Asp Asp His Arg
785                 790                 795


<210> 113
<211> 786
<212> PRT
<213> Homo sapiens

<400> 113
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
                245                 250                 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300
Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305                 310                 315                 320
Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
                325                 330                 335
Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp Arg Ile Pro Gln
            340                 345                 350
Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu Glu Thr Met Pro
        355                 360                 365
```

```
Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser
    370                 375                 380
Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Ser Thr Lys Ala
385                 390                 395                 400
Ile Val Glu Pro Glu Lys Thr Thr Ala Glu Phe Glu Val Pro Arg Leu
                405                 410                 415
Val Leu Ala Asp Ser Gly Phe Trp Glu Cys Arg Val Ser Thr Ser Gly
            420                 425                 430
Gly Gln Asp Ser Arg Arg Phe Lys Val Asn Val Lys Val Pro Pro Val
        435                 440                 445
Pro Leu Ala Ala Pro Arg Leu Leu Thr Lys Gln Ser Arg Gln Leu Val
    450                 455                 460
Val Ser Pro Leu Val Ser Phe Ser Gly Asp Gly Pro Ile Ser Thr Val
465                 470                 475                 480
Arg Leu His Tyr Arg Pro Gln Asp Ser Thr Met Asp Trp Ser Thr Ile
                485                 490                 495
Val Val Asp Pro Ser Glu Asn Val Thr Leu Met Asn Leu Arg Pro Lys
            500                 505                 510
Thr Gly Tyr Ser Val Arg Val Gln Leu Ser Arg Pro Gly Glu Gly Gly
        515                 520                 525
Glu Gly Ala Trp Gly Pro Pro Thr Leu Met Thr Thr Asp Cys Pro Glu
    530                 535                 540
Pro Leu Leu Gln Pro Trp Leu Glu Gly Trp His Val Glu Gly Thr Asp
545                 550                 555                 560
Arg Leu Arg Val Ser Trp Ser Leu Pro Leu Val Pro Gly Pro Leu Val
                565                 570                 575
Gly Asp Gly Phe Leu Leu Arg Leu Trp Asp Gly Thr Arg Gly Gln Glu
            580                 585                 590
Arg Arg Glu Asn Val Ser Ser Pro Gln Ala Arg Thr Ala Leu Leu Thr
        595                 600                 605
Gly Leu Thr Pro Gly Thr His Tyr Gln Leu Asp Val Gln Leu Tyr His
    610                 615                 620
Cys Thr Leu Leu Gly Pro Ala Ser Pro Pro Ala His Val Leu Leu Pro
625                 630                 635                 640
Pro Ser Gly Pro Pro Ala Pro Arg His Leu His Ala Gln Ala Leu Ser
                645                 650                 655
Asp Ser Glu Ile Gln Leu Thr Trp Lys His Pro Glu Ala Leu Pro Gly
            660                 665                 670
Pro Ile Ser Lys Tyr Val Val Glu Val Gln Val Ala Gly Gly Ala Gly
        675                 680                 685
Asp Pro Leu Trp Ile Asp Val Asp Arg Pro Glu Glu Thr Ser Thr Ile
    690                 695                 700
Ile Arg Gly Leu Asn Ala Ser Thr Arg Tyr Leu Phe Arg Met Arg Ala
705                 710                 715                 720
Ser Ile Gln Gly Leu Gly Asp Trp Ser Asn Thr Val Glu Glu Ser Thr
                725                 730                 735
Leu Gly Asn Gly Leu Gln Ala Glu Gly Pro Val Gln Glu Ser Arg Ala
            740                 745                 750
Ala Glu Glu Gly Leu Asp Gln Gln Leu Ile Leu Ala Val Val Gly Ser
        755                 760                 765
Val Ser Ala Thr Cys Leu Thr Ile Leu Ala Ala Leu Leu Thr Leu Val
    770                 775                 780
Cys Ile
785
```

<210> 114
<211> 984
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (37)...(897)
<223> SR005_A11

<400> 114

```
tgcccccacc cccttaggcc cgagggatca ggagct atg gga cca gag gcc ctg   54
                                        Met Gly Pro Glu Ala Leu
                                         1               5

tca tct tta ctg ctg ctg ctc ttg gtg gca agt gga gat gct gac atg   102
Ser Ser Leu Leu Leu Leu Leu Val Ala Ser Gly Asp Ala Asp Met
            10                  15                  20

aag gga cat ttt gat cct gcc aag tgc cgc tat gcc ctg ggc atg cag   150
Lys Gly His Phe Asp Pro Ala Lys Cys Arg Tyr Ala Leu Gly Met Gln
        25                  30                  35

gac cgg acc atc cca gac agt gac atc tct gct tcc agc tcc tgg tca   198
Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser Ala Ser Ser Ser Trp Ser
    40                  45                  50

gat tcc act gcc gcc cgc cac agc agg ttg gag agc agt gac ggg gat   246
Asp Ser Thr Ala Ala Arg His Ser Arg Leu Glu Ser Ser Asp Gly Asp
55                  60                  65                  70

ggg gcc tgg tgc ccc gca ggg tcg gtg ttt ccc aag gag gag gag tac   294
Gly Ala Trp Cys Pro Ala Gly Ser Val Phe Pro Lys Glu Glu Glu Tyr
                75                  80                  85

ttg cag gtg gat cta caa cga ctg cac ctg gtg gct ctg gtg ggc acc   342
Leu Gln Val Asp Leu Gln Arg Leu His Leu Val Ala Leu Val Gly Thr
            90                  95                  100

cag gga cgg cat gcc ggg ggc ctg ggc aag gag ttc tcc cgg agc tac   390
Gln Gly Arg His Ala Gly Gly Leu Gly Lys Glu Phe Ser Arg Ser Tyr
        105                 110                 115

cgg ctg cgt tac tcc cgg gat ggt cgc cgc tgg atg ggc tgg aag gac   438
Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg Trp Met Gly Trp Lys Asp
    120                 125                 130

cgc tgg ggt cag gag gtg atc tca ggc aat gag gac cct gag gga gtg   486
Arg Trp Gly Gln Glu Val Ile Ser Gly Asn Glu Asp Pro Glu Gly Val
135                 140                 145                 150

gtg ctg aag gac ctt ggg ccc ccc atg gtt gcc cga ctg gtt cgc ttc   534
Val Leu Lys Asp Leu Gly Pro Pro Met Val Ala Arg Leu Val Arg Phe
                155                 160                 165

tac ccc cgg gct gac cgg gtc atg agc gtc tgt ctg cgg gta gag ctc   582
```

```
Tyr Pro Arg Ala Asp Arg Val Met Ser Val Cys Leu Arg Val Glu Leu
            170                 175                 180

tat ggc tgc ctc tgg agg gat gga ctc ctg tct tac acc gcc cct gtg   630
Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu Ser Tyr Thr Ala Pro Val
        185                 190                 195

ggg cag aca atg tat tta tct gag gcc gtg tac ctc aac gac tcc acc   678
Gly Gln Thr Met Tyr Leu Ser Glu Ala Val Tyr Leu Asn Asp Ser Thr
    200                 205                 210

tat gac gga cat acc gtg ggc gga ctg cag tat ggg ggt ctg ggc cag   726
Tyr Asp Gly His Thr Val Gly Gly Leu Gln Tyr Gly Gly Leu Gly Gln
215                 220                 225                 230

ctg gca gat ggt gtg gtg ggg ctg gat gac ttt agg aag agt cag gag   774
Leu Ala Asp Gly Val Val Gly Leu Asp Asp Phe Arg Lys Ser Gln Glu
                235                 240                 245

ctg cgg gtc tgg cca ggc tat gac tat gtg gga tgg agc aac cac agc   822
Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val Gly Trp Ser Asn His Ser
            250                 255                 260

ttc tcc agt ggc tat gtg gag atg gag ttt gag ttt gac cgg ctg agg   870
Phe Ser Ser Gly Tyr Val Glu Met Glu Phe Glu Phe Asp Arg Leu Arg
        265                 270                 275

gcc ttc cag gct atg cag atg tgg tga acaattcctc tccggcactg         917
Ala Phe Gln Ala Met Gln Met Trp  *
    280                 285

ggaggcacct tcccgccagc cccctggtgg ccgcctggcc cacctcccac caacttcagc 977
agcttgg                                                           984

<210> 115
<211> 286
<212> PRT
<213> Homo Sapiens

<400> 115
Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
 1               5                  10                  15
Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
            20                  25                  30
Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
        35                  40                  45
Ala Ser Ser Ser Trp Ser Asp Ser Thr Ala Ala Arg His Ser Arg Leu
    50                  55                  60
Glu Ser Ser Asp Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65                  70                  75                  80
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
                85                  90                  95
Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys
            100                 105                 110
Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
        115                 120                 125
```

```
Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
    130                 135                 140
Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145                 150                 155                 160
Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Val Met Ser Val
                165                 170                 175
Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu
            180                 185                 190
Ser Tyr Thr Ala Pro Val Gly Gln Thr Met Tyr Leu Ser Glu Ala Val
        195                 200                 205
Tyr Leu Asn Asp Ser Thr Tyr Asp Gly His Thr Val Gly Gly Leu Gln
    210                 215                 220
Tyr Gly Gly Leu Gly Gln Leu Ala Asp Gly Val Val Gly Leu Asp Asp
225                 230                 235                 240
Phe Arg Lys Ser Gln Glu Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val
                245                 250                 255
Gly Trp Ser Asn His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe
            260                 265                 270
Glu Phe Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Met Trp
        275                 280                 285


<210> 116
<211> 788
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (37)...(768)

<400> 116
tgcccccacc cccttaggcc cgagggatca ggagct atg gga cca gag gcc ctg   54
                                        Met Gly Pro Glu Ala Leu
                                         1               5

tca tct tta ctg ctg ctg ctc ttg gtg gca agt gga gat gct gac atg   102
Ser Ser Leu Leu Leu Leu Leu Leu Val Ala Ser Gly Asp Ala Asp Met
             10                  15                  20

aag gga cat ttt gat cct gcc aag tgc cgc tat gcc ctg ggc atg cag   150
Lys Gly His Phe Asp Pro Ala Lys Cys Arg Tyr Ala Leu Gly Met Gln
         25                  30                  35

gac cgg acc atc cca gac agt gac atc tct gct tcc agc tcc tgg tca   198
Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser Ala Ser Ser Ser Trp Ser
     40                  45                  50

gat tcc act gcc gcc cgc cac agc agg ttg gag agc agt gac ggg gat   246
Asp Ser Thr Ala Ala Arg His Ser Arg Leu Glu Ser Ser Asp Gly Asp
 55                  60                  65                  70

ggg gcc tgg tgc ccc gca ggg tcg gtg ttt ccc aag gag gag gag tac   294
Gly Ala Trp Cys Pro Ala Gly Ser Val Phe Pro Lys Glu Glu Glu Tyr
                 75                  80                  85
```

```
ttg cag gtg gat cta caa cga ctg cac ctg gtg gct ctg gtg ggc acc   342
Leu Gln Val Asp Leu Gln Arg Leu His Leu Val Ala Leu Val Gly Thr
            90                  95                  100

cag gga cgg cat gcc ggg ggc ctg ggc aag gag ttc tcc cgg agc tac   390
Gln Gly Arg His Ala Gly Gly Leu Gly Lys Glu Phe Ser Arg Ser Tyr
        105                 110                 115

cgg ctg cgt tac tcc cgg gat ggt cgc cgc tgg atg ggc tgg aag gac   438
Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg Trp Met Gly Trp Lys Asp
    120                 125                 130

cgc tgg ggt cag gag gtg atc tca ggc aat gag gac cct gag gga gtg   486
Arg Trp Gly Gln Glu Val Ile Ser Gly Asn Glu Asp Pro Glu Gly Val
135                 140                 145                 150

gtg ctg aag gac ctt ggg ccc ccc atg gtt gcc cga ctg gtt cgc ttc   534
Val Leu Lys Asp Leu Gly Pro Pro Met Val Ala Arg Leu Val Arg Phe
                155                 160                 165

tac ccc cgg gct gac cgg gtc atg agc gtc tgt ctg cgg gta gag ctc   582
Tyr Pro Arg Ala Asp Arg Val Met Ser Val Cys Leu Arg Val Glu Leu
            170                 175                 180

tat ggc tgc ctc tgg agg gac tgc agt atg ggg gtc tgg gcc agc tgg   630
Tyr Gly Cys Leu Trp Arg Asp Cys Ser Met Gly Val Trp Ala Ser Trp
        185                 190                 195

cag atg gtg tgg tgg ggc tgg atg act tta gga aga gtc agg agc tgc   678
Gln Met Val Trp Trp Gly Trp Met Thr Leu Gly Arg Val Arg Ser Cys
    200                 205                 210

ggg tct ggc cag gct atg act atg tgg gat gga gca acc aca gct tct   726
Gly Ser Gly Gln Ala Met Thr Met Trp Asp Gly Ala Thr Thr Ala Ser
215                 220                 225                 230

cca gtg gct atg tgg aga tgg agt ttg agt ttg acc ggc tga           768
Pro Val Ala Met Trp Arg Trp Ser Leu Ser Leu Thr Gly  *
                235                 240

gggccttcca ggctatgcag                                            788

<210> 117
<211> 243
<212> PRT
<213> Homo Sapiens

<400> 117
Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
 1               5                  10                  15
Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
            20                  25                  30
Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
        35                  40                  45
Ala Ser Ser Ser Trp Ser Asp Ser Thr Ala Ala Arg His Ser Arg Leu
    50                  55                  60
```

```
Glu Ser Ser Asp Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65                  70                  75                  80
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
                85                  90                  95
Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys
            100                 105                 110
Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
        115                 120                 125
Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
    130                 135                 140
Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145                 150                 155                 160
Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Val Met Ser Val
                165                 170                 175
Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Cys Ser Met
            180                 185                 190
Gly Val Trp Ala Ser Trp Gln Met Val Trp Trp Gly Trp Met Thr Leu
        195                 200                 205
Gly Arg Val Arg Ser Cys Gly Ser Gly Gln Ala Met Thr Met Trp Asp
    210                 215                 220
Gly Ala Thr Thr Ala Ser Pro Val Ala Met Trp Arg Trp Ser Leu Ser
225                 230                 235                 240
Leu Thr Gly
```

<210> 118
<211> 878
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (9)...(695)

<400> 118

```
gaactggg atg tgg agc tgg aag tgc ctc ctc ttc tgg gct gtg ctg gtc  50
         Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val
          1               5                  10

aca gcc aca ctc tgc acc gct agg ccg tcc ccg acc ttg cct gaa caa   98
Thr Ala Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln
 15                  20                  25                  30

gat gct ctc ccc tcc tcg gag gat gat gat gat gat gat gac tcc tct   146
Asp Ala Leu Pro Ser Ser Glu Asp Asp Asp Asp Asp Asp Asp Ser Ser
                 35                  40                  45

tca gag gag aaa gaa aca gat aac acc aaa cca aac ccc gta gct cca   194
Ser Glu Glu Lys Glu Thr Asp Asn Thr Lys Pro Asn Pro Val Ala Pro
             50                  55                  60

tat tgg aca tcc cca gaa aag atg gaa aag aaa ttg cat gca gtg ccg   242
Tyr Trp Thr Ser Pro Glu Lys Met Glu Lys Lys Leu His Ala Val Pro
         65                  70                  75
```

```
gct gcc aag aca gtg aag ttc aaa tgc cct tcc agt ggg acc cca aac   290
Ala Ala Lys Thr Val Lys Phe Lys Cys Pro Ser Ser Gly Thr Pro Asn
     80                  85                  90

ccc aca ctg cgc tgg ttg aaa aat ggc aaa gaa ttc aaa cct gac cac   338
Pro Thr Leu Arg Trp Leu Lys Asn Gly Lys Glu Phe Lys Pro Asp His
 95                 100                 105                 110

aga att gga ggc tac aag gtc cgt tat gcc acc tgg agc atc ata atg   386
Arg Ile Gly Gly Tyr Lys Val Arg Tyr Ala Thr Trp Ser Ile Ile Met
                115                 120                 125

gac tct gtg gtg ccc tct gac aag ggc aac tac acc tgc att gtg gag   434
Asp Ser Val Val Pro Ser Asp Lys Gly Asn Tyr Thr Cys Ile Val Glu
            130                 135                 140

aat gag tac ggc agc atc aac cac aca tac cag ctg gat gtc gtg gag   482
Asn Glu Tyr Gly Ser Ile Asn His Thr Tyr Gln Leu Asp Val Val Glu
        145                 150                 155

cgg tcc cct cac cgg ccc atc ctg caa gca ggg ttg ccc gcc aac aaa   530
Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro Ala Asn Lys
    160                 165                 170

aca gtg gcc ctg ggt agc aac gtg gag ttc atg tgt aag gtg tac agt   578
Thr Val Ala Leu Gly Ser Asn Val Glu Phe Met Cys Lys Val Tyr Ser
175                 180                 185                 190

gac ccg cag ccg cac atc cag tgg cta aag cac atc gag gtg aat ggg   626
Asp Pro Gln Pro His Ile Gln Trp Leu Lys His Ile Glu Val Asn Gly
                195                 200                 205

agc aag att ggc cca gac aac ctg cct tat gtc cag atc ttg aag ccc   674
Ser Lys Ile Gly Pro Asp Asn Leu Pro Tyr Val Gln Ile Leu Lys Pro
            210                 215                 220

tgg aag aga ggc cgg cag tga tgacctcgcc cctgtacctg gagatcatca      725
Trp Lys Arg Gly Arg Gln  *
        225

tctattgcac aggggccttc ctcatctcct gcatggtggg gtcggtcatc gtctacaaga 785
tgaagagtgg taccaagaag agtgacttcc acagccagat ggctgtgcac aagctggcca 845
agagcatccc tctgcgcaga caggtaacag aaa                              878

<210> 119
<211> 228
<212> PRT
<213> Homo Sapiens

<400> 119
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
 1               5                  10                  15
Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Asp Ala
            20                  25                  30
Leu Pro Ser Ser Glu Asp Asp Asp Asp Asp Asp Asp Ser Ser Ser Glu
        35                  40                  45
```

```
Glu Lys Glu Thr Asp Asn Thr Lys Pro Asn Pro Val Ala Pro Tyr Trp
    50                  55                  60
Thr Ser Pro Glu Lys Met Glu Lys Lys Leu His Ala Val Pro Ala Ala
65                  70                  75                  80
Lys Thr Val Lys Phe Lys Cys Pro Ser Ser Gly Thr Pro Asn Pro Thr
                85                  90                  95
Leu Arg Trp Leu Lys Asn Gly Lys Glu Phe Lys Pro Asp His Arg Ile
            100                 105                 110
Gly Gly Tyr Lys Val Arg Tyr Ala Thr Trp Ser Ile Ile Met Asp Ser
        115                 120                 125
Val Val Pro Ser Asp Lys Gly Asn Tyr Thr Cys Ile Val Glu Asn Glu
    130                 135                 140
Tyr Gly Ser Ile Asn His Thr Tyr Gln Leu Asp Val Val Glu Arg Ser
145                 150                 155                 160
Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro Ala Asn Lys Thr Val
                165                 170                 175
Ala Leu Gly Ser Asn Val Glu Phe Met Cys Lys Val Tyr Ser Asp Pro
            180                 185                 190
Gln Pro His Ile Gln Trp Leu Lys His Ile Glu Val Asn Gly Ser Lys
        195                 200                 205
Ile Gly Pro Asp Asn Leu Pro Tyr Val Gln Ile Leu Lys Pro Trp Lys
    210                 215                 220
Arg Gly Arg Gln
225
```

<210> 120
<211> 1775
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (26)...(1366)

<400> 120

```
ggtccctgag agctgtgaga aggag atg cgg ctg ctg ctg gcc ctg ttg ggg   52
                            Met Arg Leu Leu Leu Ala Leu Leu Gly
                             1               5

gtc ctg ctg agt gtg cct ggg cct cca gtc ttg tcc ctg gag gcc tct   100
Val Leu Leu Ser Val Pro Gly Pro Pro Val Leu Ser Leu Glu Ala Ser
 10                  15                  20                  25

gag gaa gtg gag ctt gag ccc tgc ctg gct ccc agc ctg gag cag caa   148
Glu Glu Val Glu Leu Glu Pro Cys Leu Ala Pro Ser Leu Glu Gln Gln
                 30                  35                  40

gag cag gag ctg aca gta gcc ctt ggg cag cct gtg cgt ctg tgc tgt   196
Glu Gln Glu Leu Thr Val Ala Leu Gly Gln Pro Val Arg Leu Cys Cys
             45                  50                  55

ggg cgg gct gag cgt ggt ggc cac tgg tac aag gag ggc agt cgc ctg   244
Gly Arg Ala Glu Arg Gly Gly His Trp Tyr Lys Glu Gly Ser Arg Leu
         60                  65                  70
```

```
gca cct gct ggc cgt gta cgg ggc tgg agg ggc cgc cta gag att gcc   292
Ala Pro Ala Gly Arg Val Arg Gly Trp Arg Gly Arg Leu Glu Ile Ala
     75                  80                  85

agc ttc cta cct gag gat gct ggc cgc tac ctc tgc ctg gca cga ggc   340
Ser Phe Leu Pro Glu Asp Ala Gly Arg Tyr Leu Cys Leu Ala Arg Gly
 90                  95                 100                 105

tcc atg atc gtc ctg cag aat ctc acc ttg att aca ggt gac tcc ttg   388
Ser Met Ile Val Leu Gln Asn Leu Thr Leu Ile Thr Gly Asp Ser Leu
                110                 115                 120

acc tcc agc aac gat gat gag gac ccc aag tcc cat agg gac ccc tcg   436
Thr Ser Ser Asn Asp Asp Glu Asp Pro Lys Ser His Arg Asp Pro Ser
            125                 130                 135

aat agg cac agt tac ccc cag caa gca ccc tac tgg aca cac ccc cag   484
Asn Arg His Ser Tyr Pro Gln Gln Ala Pro Tyr Trp Thr His Pro Gln
        140                 145                 150

cgc atg gag aag aaa ctg cat gca gta cct gcg ggg aac acc gtc aag   532
Arg Met Glu Lys Lys Leu His Ala Val Pro Ala Gly Asn Thr Val Lys
    155                 160                 165

ttc cgc tgt cca gct gca ggc aac ccc acg ccc acc atc cgc tgg ctt   580
Phe Arg Cys Pro Ala Ala Gly Asn Pro Thr Pro Thr Ile Arg Trp Leu
170                 175                 180                 185

aag gat gga cag gcc ttt cat ggg gag aac cgc att gga ggc att cgg   628
Lys Asp Gly Gln Ala Phe His Gly Glu Asn Arg Ile Gly Gly Ile Arg
                190                 195                 200

ctg cgc cat cag cac tgg agt ctc gtg atg gag agc gtg gtg ccc tcg   676
Leu Arg His Gln His Trp Ser Leu Val Met Glu Ser Val Val Pro Ser
            205                 210                 215

gac cgc ggc aca tac acc tgc ctg gta gag aac gct gtg ggc agc atc   724
Asp Arg Gly Thr Tyr Thr Cys Leu Val Glu Asn Ala Val Gly Ser Ile
        220                 225                 230

cgc tat aac tac ctg cta gat gtg ctg gag cgg tcc ccg cac cgg ccc   772
Arg Tyr Asn Tyr Leu Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro
    235                 240                 245

atc ctg cag gcc ggg ctc ccg gcc aac acc aca gcc gtg gtg ggc agc   820
Ile Leu Gln Ala Gly Leu Pro Ala Asn Thr Thr Ala Val Val Gly Ser
250                 255                 260                 265

gac gtg gag ctg ctg tgc aag gtg tac agc gat gcc cag ccc cac atc   868
Asp Val Glu Leu Leu Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
                270                 275                 280

cag tgg ctg aag cac atc gtc atc aac ggc agc agc ttc gga gcc gac   916
Gln Trp Leu Lys His Ile Val Ile Asn Gly Ser Ser Phe Gly Ala Asp
            285                 290                 295
```

```
ggt ttc ccc tat gtg caa gtc cta aag act gca gac atc aat agc tca   964
Gly Phe Pro Tyr Val Gln Val Leu Lys Thr Ala Asp Ile Asn Ser Ser
        300                 305                 310

gag gtg gag gtc ctg tac ctg cgg aac gtg tca gcc gag gac gca ggc   1012
Glu Val Glu Val Leu Tyr Leu Arg Asn Val Ser Ala Glu Asp Ala Gly
    315                 320                 325

gag tac acc tgc ctc gca ggc aat tcc atc ggc ctc tcc tac cag tct   1060
Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser Tyr Gln Ser
330                 335                 340                 345

gcc tgg ctc acg gtg ctg cca ggt gag cac ctg aag ggc cag gag atg   1108
Ala Trp Leu Thr Val Leu Pro Gly Glu His Leu Lys Gly Gln Glu Met
                350                 355                 360

ctg cga gat gcc cct ctg ggc cag cag tgg ggg ctg tgg cct gtt ggg   1156
Leu Arg Asp Ala Pro Leu Gly Gln Gln Trp Gly Leu Trp Pro Val Gly
            365                 370                 375

tgg tca gtc tct gtt ggc ctg tgg ggt ctg gcc tgg ggg gca gtg tgt   1204
Trp Ser Val Ser Val Gly Leu Trp Gly Leu Ala Trp Gly Ala Val Cys
        380                 385                 390

gga ttt gtg ggt ttg agc tgt atg aca gcc cct ctg tgc ctc tcc aca   1252
Gly Phe Val Gly Leu Ser Cys Met Thr Ala Pro Leu Cys Leu Ser Thr
    395                 400                 405

cgt ggc cgt cca tgt gac cgt ctg ctg agg tgt ggg tgc ctg gga ctg   1300
Arg Gly Arg Pro Cys Asp Arg Leu Leu Arg Cys Gly Cys Leu Gly Leu
410                 415                 420                 425

ggc ata act aca gct tcc tcc gtg tgt gtc ccc aca tat gtt ggg agc   1348
Gly Ile Thr Thr Ala Ser Ser Val Cys Val Pro Thr Tyr Val Gly Ser
                430                 435                 440

tgg gag gga ctg agt tag ggtgcacggg gcggccagtc tcaccactga          1396
Trp Glu Gly Leu Ser  *
            445

ccagtttgtc tgtctgtgtg tgtccatgtg cgagggcaga ggaggacccc acatggaccg 1456
cagcagcgcc cgaggccagg tatacggaca tcatcctgta cgcgtcgggc tccctggcct 1516
tggctgtgct cctgctgctg gccgggctgt atcgagggca ggcgctccac ggccggcacc 1576
cccgcccgcc cgccactgtg cagaagctct cccgcttccc tctggcccga cagttctccc 1636
tggagtcagg ctcttccggc aagtcaagct catccctggt acgaggcgtg cgtctctcct 1696
ccagcggccc cgccttgctc gccggcctcg tgagtctaga tctacctctc gacccactat 1756
gggagttccc ccgggacag                                              1775

<210> 121
<211> 446
<212> PRT
<213> Homo Sapiens

<400> 121
Met Arg Leu Leu Leu Ala Leu Leu Gly Val Leu Leu Ser Val Pro Gly
 1               5                  10                  15
```

```
Pro Pro Val Leu Ser Leu Glu Ala Ser Glu Glu Val Glu Leu Glu Pro
            20                  25                  30
Cys Leu Ala Pro Ser Leu Glu Gln Gln Glu Gln Glu Leu Thr Val Ala
        35                  40                  45
Leu Gly Gln Pro Val Arg Leu Cys Cys Gly Arg Ala Glu Arg Gly Gly
    50                  55                  60
His Trp Tyr Lys Glu Gly Ser Arg Leu Ala Pro Ala Gly Arg Val Arg
65                  70                  75                  80
Gly Trp Arg Gly Arg Leu Glu Ile Ala Ser Phe Leu Pro Glu Asp Ala
                85                  90                  95
Gly Arg Tyr Leu Cys Leu Ala Arg Gly Ser Met Ile Val Leu Gln Asn
            100                 105                 110
Leu Thr Leu Ile Thr Gly Asp Ser Leu Thr Ser Ser Asn Asp Asp Glu
        115                 120                 125
Asp Pro Lys Ser His Arg Asp Pro Ser Asn Arg His Ser Tyr Pro Gln
    130                 135                 140
Gln Ala Pro Tyr Trp Thr His Pro Gln Arg Met Glu Lys Lys Leu His
145                 150                 155                 160
Ala Val Pro Ala Gly Asn Thr Val Lys Phe Arg Cys Pro Ala Ala Gly
                165                 170                 175
Asn Pro Thr Pro Thr Ile Arg Trp Leu Lys Asp Gly Gln Ala Phe His
            180                 185                 190
Gly Glu Asn Arg Ile Gly Gly Ile Arg Leu Arg His Gln His Trp Ser
        195                 200                 205
Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly Thr Tyr Thr Cys
    210                 215                 220
Leu Val Glu Asn Ala Val Gly Ser Ile Arg Tyr Asn Tyr Leu Leu Asp
225                 230                 235                 240
Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro
                245                 250                 255
Ala Asn Thr Thr Ala Val Val Gly Ser Asp Val Glu Leu Leu Cys Lys
            260                 265                 270
Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu Lys His Ile Val
        275                 280                 285
Ile Asn Gly Ser Ser Phe Gly Ala Asp Gly Phe Pro Tyr Val Gln Val
    290                 295                 300
Leu Lys Thr Ala Asp Ile Asn Ser Ser Glu Val Glu Val Leu Tyr Leu
305                 310                 315                 320
Arg Asn Val Ser Ala Glu Asp Ala Gly Glu Tyr Thr Cys Leu Ala Gly
                325                 330                 335
Asn Ser Ile Gly Leu Ser Tyr Gln Ser Ala Trp Leu Thr Val Leu Pro
            340                 345                 350
Gly Glu His Leu Lys Gly Gln Glu Met Leu Arg Asp Ala Pro Leu Gly
        355                 360                 365
Gln Gln Trp Gly Leu Trp Pro Val Gly Trp Ser Val Ser Val Gly Leu
    370                 375                 380
Trp Gly Leu Ala Trp Gly Ala Val Cys Gly Phe Val Gly Leu Ser Cys
385                 390                 395                 400
Met Thr Ala Pro Leu Cys Leu Ser Thr Arg Gly Arg Pro Cys Asp Arg
                405                 410                 415
Leu Leu Arg Cys Gly Cys Leu Gly Leu Gly Ile Thr Thr Ala Ser Ser
            420                 425                 430
Val Cys Val Pro Thr Tyr Val Gly Ser Trp Glu Gly Leu Ser
        435                 440                 445
```

<210> 122
<211> 923
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (253)...(777)

<400> 122
gcggacactc ctctcggctc ctccccggca gcggcggcgg ctcggagcgg gctccggggc 60
tcgggtgcag cggccagcgg gcgcctggcg gcgaggatta cccggggaag tggttgtctc 120
ctggctggag ccgcgagacg ggcgctcagg gcgcggggcc ggcggcggcg aacgagagga 180
cggactctgg cggccgggtc gttggccgcg gggagcgcgg gcaccgggcg agcaggccgc 240
gtcgcgctca cc atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg 291
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala
1 5 10

ctg ctc agc tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta 339
Leu Leu Ser Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu
15 20 25

aaa gat cct gaa ctg agt tta aaa ggc acc cag cac atc atg caa gca 387
Lys Asp Pro Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala
30 35 40 45

ggc cag aca ctg cat ctc caa tgc agg ggg gaa gca gcc cat aaa tgg 435
Gly Gln Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp
50 55 60

tct ttg cct gaa atg gtg agt aag gaa agc gaa agg ctg agc ata act 483
Ser Leu Pro Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr
65 70 75

aaa tct gcc tgt gga aga aat ggc aaa caa ttc tgc agt act tta acc 531
Lys Ser Ala Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr
80 85 90

ttg aac aca gct caa gca aac cac act ggc ttc tac agc tgc aaa tat 579
Leu Asn Thr Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr
95 100 105

cta gct gta cct act tca aag aag aag gaa aca gaa tct gca atc tat 627
Leu Ala Val Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr
110 115 120 125

ata ttt att agt gat aca ggt aga cct ttc gta gag atg tac agt gaa 675
Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu
130 135 140

atc ccc gaa att ata cac atg act gaa gga agg gag ctc gtc att ccc 723
Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro
145 150 155

tgc cgg gtt acg tca cct aac atc act gtt act tta aaa aag aag aag 771
Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Lys Lys

```
        160                 165                 170

gca taa ggagaaagtc agatcatgga ttattttctt ctgtttggac tcaccgtgct    827
Ala  *


tgggaatact tctgagcatt agagagcact tcattcattg cagagtctct ggcctccgag 887
gctgccttca ccatcagcag cttcagcttc tgggag                          923

<210> 123
<211> 174
<212> PRT
<213> Homo Sapiens

<400> 123
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Lys Lys Ala
                165                 170


<210> 124
<211> 783
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (17)...(700)

<400> 124
cgcgcagcgg ccggag atg cag cgg ggc gcc gcg ctg tgc ctg cga ctg tgg 52
                  Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp
                   1               5                   10

ctc tgc ctg gga ctc ctg gac ggc ctg gtg agt ggc tac tcc atg acc   100
Leu Cys Leu Gly Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr
         15                  20                  25
```

```
ccc ccg acc ttg aac atc acg gag gag tca cac gtc atc gac acc ggt   148
Pro Pro Thr Leu Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly
     30                  35                  40

gac agc ctg tcc atc tcc tgc agg gga cag cac ccc ctc gag tgg gct   196
Asp Ser Leu Ser Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala
 45                  50                  55                  60

tgg cca gga gct cag gag gcg cca gcc acc gga gac aag gac agc gag   244
Trp Pro Gly Ala Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu
                 65                  70                  75

gac acg ggg gtg gtg cga gac tgc gag ggc aca gac gcc agg ccc tac   292
Asp Thr Gly Val Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr
             80                  85                  90

tgc aag gtg ttg ctg ctg cac gag gta cat gcc aac gac aca ggc agc   340
Cys Lys Val Leu Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser
         95                 100                 105

tac gtc tgc tac tac aag tac atc aag gca cgc atc gag ggc acc acg   388
Tyr Val Cys Tyr Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr
    110                 115                 120

gcc gcc agc tcc tac gtg ttc gtg aga gga agg acg cca tgt ggg tgc   436
Ala Ala Ser Ser Tyr Val Phe Val Arg Gly Arg Thr Pro Cys Gly Cys
125                 130                 135                 140

cct gtc tgg tgt cca tcc ccg gcc tca atg tca cgc tgc gct cgc aaa   484
Pro Val Trp Cys Pro Ser Pro Ala Ser Met Ser Arg Cys Ala Arg Lys
                145                 150                 155

gct cgg tgc tgt ggc cag acg ggc agg agg tgg tgt ggg atg acc ggc   532
Ala Arg Cys Cys Gly Gln Thr Gly Arg Arg Trp Cys Gly Met Thr Gly
            160                 165                 170

ggg gca tgc tcg tgt cca cgc cac tgc tgc acg atg ccc tgt acc tgc   580
Gly Ala Cys Ser Cys Pro Arg His Cys Cys Thr Met Pro Cys Thr Cys
        175                 180                 185

agt gcg aga cca cct ggg gag acc agg act tcc ttt cca acc cct tcc   628
Ser Ala Arg Pro Pro Gly Glu Thr Arg Thr Ser Phe Pro Thr Pro Ser
    190                 195                 200

tgg tgc aca tca cag gca acg agc tct atg aca tcc agc tgt tgc cca   676
Trp Cys Thr Ser Gln Ala Thr Ser Ser Met Thr Ser Ser Cys Cys Pro
205                 210                 215                 220

gga agt cgc tgg agc tgc tgg tag gggagaagct ggtcctgaac tgcaccgtgt  730
Gly Ser Arg Trp Ser Cys Trp  *
                225

gggctgagtt taactcaggt gtcacctttg actgggacta cccagggaag cag        783
```

<210> 125

<211> 227
<212> PRT
<213> Homo Sapiens

<400> 125
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
1 5 10 15
Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
20 25 30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
35 40 45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
50 55 60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65 70 75 80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
85 90 95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
115 120 125
Tyr Val Phe Val Arg Gly Arg Thr Pro Cys Gly Cys Pro Val Trp Cys
130 135 140
Pro Ser Pro Ala Ser Met Ser Arg Cys Ala Arg Lys Ala Arg Cys Cys
145 150 155 160
Gly Gln Thr Gly Arg Arg Trp Cys Gly Met Thr Gly Gly Ala Cys Ser
165 170 175
Cys Pro Arg His Cys Cys Thr Met Pro Cys Thr Cys Ser Ala Arg Pro
180 185 190
Pro Gly Glu Thr Arg Thr Ser Phe Pro Thr Pro Ser Trp Cys Thr Ser
195 200 205
Gln Ala Thr Ser Ser Met Thr Ser Ser Cys Cys Pro Gly Ser Arg Trp
210 215 220
Ser Cys Trp
225

<210> 126
<211> 1356
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (16)...(903)

<400> 126
gcgcagcggc cggag atg cag cgg ggc gcc gcg ctg tgc ctg cga ctg tgg 51
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp
1 5 10

ctc tgc ctg gga ctc ctg gac ggc ctg gtg agt ggc tac tcc atg acc 99
Leu Cys Leu Gly Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr
15 20 25

ccc ccg acc ttg aac atc acg gag gag tca cac gtc atc gac acc ggt 147

```
Pro Pro Thr Leu Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly
     30                  35                  40

gac agc ctg tcc atc tcc tgc agg gga cag cac ccc ctc gag tgg gct   195
Asp Ser Leu Ser Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala
 45                  50                  55                  60

tgg cca gga gct cag gag gcg cca gcc acc gga gac aag gac agc gag   243
Trp Pro Gly Ala Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu
                65                  70                  75

gac acg ggg gtg gtg cga gac tgc gag ggc aca gac gcc agg ccc tac   291
Asp Thr Gly Val Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr
            80                  85                  90

tgc aag gtg ttg ctg ctg cac gag gta cat gcc aac gac aca ggc agc   339
Cys Lys Val Leu Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser
         95                 100                 105

tac gtc tgc tac tac aag tac atc aag gca cgc atc gag ggc acc acg   387
Tyr Val Cys Tyr Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr
    110                 115                 120

gcc gcc agc tcc tac gtg ttc gtg aga gac ttt gag cag cca ttc atc   435
Ala Ala Ser Ser Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile
125                 130                 135                 140

aac aag cct gac acg ctc ttg gtc aac agg aag gac gcc atg tgg gtg   483
Asn Lys Pro Asp Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val
                145                 150                 155

ccc tgt ctg gtg tcc atc ccc ggc ctc aat gtc acg ctg cgc tcg caa   531
Pro Cys Leu Val Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln
            160                 165                 170

agc tcg gtg ctg tgg cca gac ggg cag gag gtg gtg tgg gat gac cgg   579
Ser Ser Val Leu Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg
        175                 180                 185

cgg ggc atg ctc gtg tcc acg cca ctg ctg cac gat gcc ctg tac ctg   627
Arg Gly Met Leu Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu
    190                 195                 200

cag tgc gag acc acc tgg gga gac cag gac ttc ctt tcc aac ccc ttc   675
Gln Cys Glu Thr Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe
205                 210                 215                 220

ctg gtg cac atc aca ggc aac gag ctc tat gac atc cag ctg ttg ccc   723
Leu Val His Ile Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro
                225                 230                 235

agg aag tcg ctg gag ctg ctg gta ggg gag aag ctg gtc ctg aac tgc   771
Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys
            240                 245                 250

acc gtg tgg gct gag ttt aac tca ggt gtc acc ttt gac tgg gac tac   819
```

```
Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr
        255                 260                 265

cca ggg aag cag aaa atc cct tca tca gcg tcg agt ggc tca aag gac   867
Pro Gly Lys Gln Lys Ile Pro Ser Ser Ala Ser Ser Gly Ser Lys Asp
    270                 275                 280

cca tcc tgg agg cca cgg cag gag acg agc tgg tga agctgcccgt        913
Pro Ser Trp Arg Pro Arg Gln Glu Thr Ser Trp  *
285                 290                 295

gaagctggca gcgtaccccc cgcccgagtt ccagtggtac aaggatggaa aggcactgtc 973
cgggcgccac agtccacatg ccctggtgct caaggaggtg acagaggcca gcacaggcac 1033
ctacaccctc gccctgtgga actccgctgc tggcctgagg cgcaacatca gcctggagct 1093
ggtggtgaat gtgccccccc agatacatga gaaggaggcc tcctccccca gcatctactc 1153
gcgtcacagc cgccaggccc tcacctgcac ggcctacggg gtgcccctgc ctctcagcat 1213
ccagtggcac tggcggccct ggacaccctg caagatgttt gcccagcgta gtctccggcg 1273
gcggcagcag caagacctca tgccacagtg ccgtgactgg agggcggtga ccacgcagga 1333
tgccgtgaac cccatcgaga gcc                                         1356

<210> 127
<211> 295
<212> PRT
<213> Homo Sapiens

<400> 127
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
 1               5                  10                  15
Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
            20                  25                  30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
        35                  40                  45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
    50                  55                  60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65                  70                  75                  80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
                85                  90                  95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
            100                 105                 110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
        115                 120                 125
Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
    130                 135                 140
Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145                 150                 155                 160
Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
                165                 170                 175
Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
            180                 185                 190
Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
        195                 200                 205
Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
    210                 215                 220
Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225                 230                 235                 240
```

```
Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
               245                 250                 255
Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
           260                 265                 270
Lys Ile Pro Ser Ser Ala Ser Ser Gly Ser Lys Asp Pro Ser Trp Arg
       275                 280                 285
Pro Arg Gln Glu Thr Ser Trp
   290                 295


<210> 128
<211> 1589
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (29)...(1516)

<400> 128
ggatcctcta gggtcccagc tcgcctcg atg gag ctc ctc ccg ccg ctg cct    52
                                Met Glu Leu Leu Pro Pro Leu Pro
                                 1               5

cag tcc ttc ctg ttg ctg ctg ctg ttg cct gcc aag ccc gcg gcg ggc   100
Gln Ser Phe Leu Leu Leu Leu Leu Leu Pro Ala Lys Pro Ala Ala Gly
     10                  15                  20

gag gac tgg cag tgc ccg cgc acc ccc tac gcg gcc tct cgc gac ttt   148
Glu Asp Trp Gln Cys Pro Arg Thr Pro Tyr Ala Ala Ser Arg Asp Phe
 25                  30                  35                  40

gac gtg aag tac gtg gtg ccc agc ttc tcc gcc gga ggc ctg gta cag   196
Asp Val Lys Tyr Val Val Pro Ser Phe Ser Ala Gly Gly Leu Val Gln
                 45                  50                  55

gcc atg gtg acc tac gag ggc gac aga aat gag agt gct gtg ttt gta   244
Ala Met Val Thr Tyr Glu Gly Asp Arg Asn Glu Ser Ala Val Phe Val
             60                  65                  70

gcc ata cgc aat cgc ctg cat gtg ctt ggg cct gac ctg aag tct gtc   292
Ala Ile Arg Asn Arg Leu His Val Leu Gly Pro Asp Leu Lys Ser Val
         75                  80                  85

cag agc ctg gcc acg ggc cct gct gga gac cct ggc tgc cag acg tgt   340
Gln Ser Leu Ala Thr Gly Pro Ala Gly Asp Pro Gly Cys Gln Thr Cys
     90                  95                  100

gca gcc tgt ggc cca gga ccc cac ggc cct ccc ggt gac aca gac aca   388
Ala Ala Cys Gly Pro Gly Pro His Gly Pro Pro Gly Asp Thr Asp Thr
105                 110                 115                 120

aag gtg ctg gtg ctg gat ccc gcg ctg cct gcg ctg gtc agt tgt ggc   436
Lys Val Leu Val Leu Asp Pro Ala Leu Pro Ala Leu Val Ser Cys Gly
                125                 130                 135
```

```
tcc agc ctg cag ggc cgc tgc ttc ctg cat gac cta gag ccc caa ggg   484
Ser Ser Leu Gln Gly Arg Cys Phe Leu His Asp Leu Glu Pro Gln Gly
            140                 145                 150

aca gcc gtg cat ctg gca gcg cca gcc tgc ctc ttc tca gcc cac cat   532
Thr Ala Val His Leu Ala Ala Pro Ala Cys Leu Phe Ser Ala His His
        155                 160                 165

aac cgg ccc gat gac tgc ccc gac tgt gtg gcc agc cca ttg ggc acc   580
Asn Arg Pro Asp Asp Cys Pro Asp Cys Val Ala Ser Pro Leu Gly Thr
    170                 175                 180

cgt gta act gtg gtt gag caa ggc cag gcc tcc tat ttc tac gtg gca   628
Arg Val Thr Val Val Glu Gln Gly Gln Ala Ser Tyr Phe Tyr Val Ala
185                 190                 195                 200

tcc tca ctg gac gca gcc gtg gct gcc agc ttc agc cca cgc tca gtg   676
Ser Ser Leu Asp Ala Ala Val Ala Ala Ser Phe Ser Pro Arg Ser Val
                205                 210                 215

tct atc agg cgt ctc aag gct gac gcc tcg gga ttc gca ccg ggc ttt   724
Ser Ile Arg Arg Leu Lys Ala Asp Ala Ser Gly Phe Ala Pro Gly Phe
            220                 225                 230

gtg gcg ttg tca gtg ctg ccc aag cat ctt gtc tcc tac agt att gaa   772
Val Ala Leu Ser Val Leu Pro Lys His Leu Val Ser Tyr Ser Ile Glu
        235                 240                 245

tac gtg cac agc ttc cac acg gga gcc ttc gta tac ttc ctg act gta   820
Tyr Val His Ser Phe His Thr Gly Ala Phe Val Tyr Phe Leu Thr Val
    250                 255                 260

cag ccg gcc agc gtg aca gat gat cct agt gcc ctg cac aca cgc ctg   868
Gln Pro Ala Ser Val Thr Asp Asp Pro Ser Ala Leu His Thr Arg Leu
265                 270                 275                 280

gca cgg ctt agc gcc act gag cca gag ttg ggt gac tat cgg gag ctg   916
Ala Arg Leu Ser Ala Thr Glu Pro Glu Leu Gly Asp Tyr Arg Glu Leu
                285                 290                 295

gtc ctc gac tgc aga ttt gct cca aaa cgc agg cgc cgg ggg gcc cca   964
Val Leu Asp Cys Arg Phe Ala Pro Lys Arg Arg Arg Arg Gly Ala Pro
            300                 305                 310

gaa ggc gga cag ccc tac cct gtg ctg cgg gtg gcc cac tcc gct cca   1012
Glu Gly Gly Gln Pro Tyr Pro Val Leu Arg Val Ala His Ser Ala Pro
        315                 320                 325

gtg ggt gcc caa ctt gcc act gag ctg agc atc gcc gag ggc cag gaa   1060
Val Gly Ala Gln Leu Ala Thr Glu Leu Ser Ile Ala Glu Gly Gln Glu
    330                 335                 340

gta cta ttt ggg gtc ttt gtg act ggc aag gat ggt ggt cct ggc gtg   1108
Val Leu Phe Gly Val Phe Val Thr Gly Lys Asp Gly Gly Pro Gly Val
345                 350                 355                 360
```

```
ggc ccc aac tct gtc gtc tgt gcc ttc ccc att gac ctg ctg gac aca   1156
Gly Pro Asn Ser Val Val Cys Ala Phe Pro Ile Asp Leu Leu Asp Thr
                365                 370                 375

cta att gat gag ggt gtg gag cgc tgt tgt gaa tcc cca gtc cat cca   1204
Leu Ile Asp Glu Gly Val Glu Arg Cys Cys Glu Ser Pro Val His Pro
            380                 385                 390

ggc ctc cgg cga ggc ctc gac ttc ttc cag tcg ccc agt ttt tgc ccc   1252
Gly Leu Arg Arg Gly Leu Asp Phe Phe Gln Ser Pro Ser Phe Cys Pro
        395                 400                 405

aac ccg cct ggc ctg gaa gcc ctc agc ccc aac acc agc tgc cgc cac   1300
Asn Pro Pro Gly Leu Glu Ala Leu Ser Pro Asn Thr Ser Cys Arg His
    410                 415                 420

ttc cct ctg ctg gtc agt agc agc ttc tca cgt gtg gac cta ttc aat   1348
Phe Pro Leu Leu Val Ser Ser Ser Phe Ser Arg Val Asp Leu Phe Asn
425                 430                 435                 440

ggg ctg ttg gga cca gta cag gtc act gca ttg tat gtg aca cgc ctt   1396
Gly Leu Leu Gly Pro Val Gln Val Thr Ala Leu Tyr Val Thr Arg Leu
                445                 450                 455

gac aac gtc aca gtg gca cac atg ggc aca atg gat ggg cgt atc ctg   1444
Asp Asn Val Thr Val Ala His Met Gly Thr Met Asp Gly Arg Ile Leu
            460                 465                 470

cag gtg ggt cct cat ccc cac agt ccc cta gcc ctg ggt cct tgt ctc   1492
Gln Val Gly Pro His Pro His Ser Pro Leu Ala Leu Gly Pro Cys Leu
        475                 480                 485

cat ccc cat ttt gct cac atc tga cctgtcctag gtggagctgg tcaggtcact  1546
His Pro His Phe Ala His Ile  *
    490                 495

aaactacttg ctgtatgtgt ccaacttctc actgggtgac agt                   1589
```

<210> 129
<211> 495
<212> PRT
<213> Homo Sapiens

<400> 129

```
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1               5                  10                  15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20                  25                  30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35                  40                  45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50                  55                  60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65                  70                  75                  80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85                  90                  95
```

```
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100                 105                 110
Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115                 120                 125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145                 150                 155                 160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205
Ala Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Arg Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415
Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
            420                 425                 430
Phe Ser Arg Val Asp Leu Phe Asn Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445
Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460
Gly Thr Met Asp Gly Arg Ile Leu Gln Val Gly Pro His Pro His Ser
465                 470                 475                 480
Pro Leu Ala Leu Gly Pro Cys Leu His Pro His Phe Ala His Ile
                485                 490                 495
```

<210> 130
<211> 1505
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (41)...(1144)

<400> 130
tgcacatttg tggaaactgg atggagagat ttggggaagc atg gac tct tta gcc 55
Met Asp Ser Leu Ala
1 5

agc tta gtt ctc tgt gga gtc agc ttg ctc ctt tct gga act gtg gaa 103
Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu Ser Gly Thr Val Glu
10 15 20

ggt gcc atg gac ttg atc ttg atc aat tcc cta cct ctt gta tct gat 151
Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu Pro Leu Val Ser Asp
25 30 35

gct gaa aca tct ctc acc tgc att gcc tct ggg tgg cgc ccc cat gag 199
Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly Trp Arg Pro His Glu
40 45 50

ccc atc acc ata gga agg gac ttt gaa gcc tta atg aac cag cac cag 247
Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu Met Asn Gln His Gln
55 60 65

gat ccg ctg gaa gtt act caa gat gtg acc aga gaa tgg gct aaa aaa 295
Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg Glu Trp Ala Lys Lys
70 75 80 85

gtt gtt tgg aag aga gaa aag gct agt aag atc aat ggt gct tat ttc 343
Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile Asn Gly Ala Tyr Phe
90 95 100

tgt gaa ggg cga gtt cga gga gag gca atc agg ata cga acc atg aag 391
Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg Ile Arg Thr Met Lys
105 110 115

atg cgt caa caa gct tcc ttc cta cca gct act tta act atg act gtg 439
Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr Leu Thr Met Thr Val
120 125 130

gac aag gga gat aac gtg aac ata tct ttc aaa aag gta ttg att aaa 487
Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys Lys Val Leu Ile Lys
135 140 145

gaa gaa gat gca gtg att tac aaa aat ggt tcc ttc atc cat tca gtg 535
Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser Phe Ile His Ser Val
150 155 160 165

ccc cgg cat gaa gta cct gat att cta gaa gta cac ctg cct cat gct 583
Pro Arg His Glu Val Pro Asp Ile Leu Glu Val His Leu Pro His Ala
170 175 180

cag ccc cag gat gct gga gtg tac tcg gcc agg tat ata gga gga aac 631
Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg Tyr Ile Gly Gly Asn

```
            185                 190                 195

ctc ttc acc tcg gcc ttc acc agg ctg ata gtc cgg aga tgt gaa gcc   679
Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val Arg Arg Cys Glu Ala
        200                 205                 210

cag aag tgg gga cct gaa tgc aac cat ctc tgt act gct tgt atg aac   727
Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys Thr Ala Cys Met Asn
    215                 220                 225

aat ggt gtc tgc cat gaa gat act gga gaa tgc att tgc cct cct ggg   775
Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys Ile Cys Pro Pro Gly
230                 235                 240                 245

ttt atg gga agg acg tgt gag aag gct tgt gaa ctg cac acg ttt ggc   823
Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu Leu His Thr Phe Gly
                250                 255                 260

aga act tgt aaa gaa agg tgc agt gga caa gag gga tgc aag tct tat   871
Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu Gly Cys Lys Ser Tyr
            265                 270                 275

gtg ttc tgt ctc cct gac ccc tat ggg tgt tcc tgt gcc aca ggc tgg   919
Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser Cys Ala Thr Gly Trp
        280                 285                 290

aag ggt ctg cag tgc aat gaa gca tgc cac cct ggt ttt tac ggg cca   967
Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro Gly Phe Tyr Gly Pro
    295                 300                 305

gat tgt aag ctt agg tgc agc tgc aac aat ggg gag atg tgt gat cgc   1015
Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly Glu Met Cys Asp Arg
310                 315                 320                 325

ttc caa gga tgt ctc tgc tct cca gga tgg cag ggg ctc cag tgt gag   1063
Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln Gly Leu Gln Cys Glu
                330                 335                 340

aga gaa ggt aaa gca agg cat aca gag gat gac ccc aaa gat agt gga   1111
Arg Glu Gly Lys Ala Arg His Thr Glu Asp Asp Pro Lys Asp Ser Gly
            345                 350                 355

ttt gcc aga tca tat aga agt aaa cag tgg taa atttaatccc atttgcaaag 1164
Phe Ala Arg Ser Tyr Arg Ser Lys Gln Trp  *
        360                 365

cttctggctg gccgctacct actaatgaag aaatgaccct ggtgaagccg gatgggacag 1224
tgctccatta gccatattca ccatccaccg gatcctcccc cctgactcag gagtttgggt 1284
ctgcagtgtg aacacagtgg ctgggatggt ggaaaagccc ttcaacattt ctgttaaagt 1344
tcttccaaag cccctgaatg ccccaaacgt gattgacact ggacataact ttgctgtcat 1404
caacatcagc tctgagcctt actttgggga tggaccaatc aaatccaaga agcttctata 1464
caaacccgtt aatcactatg aggcttggca acatattcaa g                     1505

<210> 131
<211> 367
<212> PRT
```

<213> Homo Sapiens

<400> 131

```
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
    290                 295                 300
Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305                 310                 315                 320
Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
                325                 330                 335
Gly Leu Gln Cys Glu Arg Glu Gly Lys Ala Arg His Thr Glu Asp Asp
            340                 345                 350
Pro Lys Asp Ser Gly Phe Ala Arg Ser Tyr Arg Ser Lys Gln Trp
        355                 360                 365
```

<210> 132
<211> 1467
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (41)...(1447)

<400> 132
tgcacatttg tggaaactgg atggagagat ttggggaagc atg gac tct tta gcc 55
Met Asp Ser Leu Ala
1 5

agc tta gtt ctc tgt gga gtc agc ttg ctc ctt tct gga act gtg gaa 103
Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu Ser Gly Thr Val Glu
10 15 20

ggt gcc atg gac ttg atc ttg atc aat tcc cta cct ctt gta tct gat 151
Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu Pro Leu Val Ser Asp
25 30 35

gct gaa aca tct ctc acc tgc att gcc tct ggg tgg cgc ccc cat gag 199
Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly Trp Arg Pro His Glu
40 45 50

ccc atc acc ata gga agg gac ttt gaa gcc tta atg aac cag cac cag 247
Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu Met Asn Gln His Gln
55 60 65

gat ccg ctg gaa gtt act caa gat gtg acc aga gaa tgg gct aaa aaa 295
Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg Glu Trp Ala Lys Lys
70 75 80 85

gtt gtt tgg aag aga gaa aag gct agt aag atc aat ggt gct tat ttc 343
Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile Asn Gly Ala Tyr Phe
90 95 100

tgt gaa ggg cga gtt cga gga gag gca atc agg ata cga acc atg aag 391
Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg Ile Arg Thr Met Lys
105 110 115

atg cgt caa caa gct tcc ttc cta cca gct act tta act atg act gtg 439
Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr Leu Thr Met Thr Val
120 125 130

gac aag gga gat aac gtg aac ata tct ttc aaa aag gta ttg att aaa 487
Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys Lys Val Leu Ile Lys
135 140 145

gaa gaa gat gca gtg att tac aaa aat ggt tcc ttc atc cat tca gtg 535
Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser Phe Ile His Ser Val
150 155 160 165

ccc cgg cat gaa gta cct gat att cta gaa gta cac ctg cct cat gct 583
Pro Arg His Glu Val Pro Asp Ile Leu Glu Val His Leu Pro His Ala
170 175 180

cag ccc cag gat gct gga gtg tac tcg gcc agg tat ata gga gga aac 631
Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg Tyr Ile Gly Gly Asn
185 190 195

```
ctc ttc acc tcg gcc ttc acc agg ctg ata gtc cgg aga tgt gaa gcc   679
Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val Arg Arg Cys Glu Ala
        200                 205                 210

cag aag tgg gga cct gaa tgc aac cat ctc tgt act gct tgt atg aac   727
Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys Thr Ala Cys Met Asn
    215                 220                 225

aat ggt gtc tgc cat gaa gat act gga gaa tgc att tgc cct cct ggg   775
Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys Ile Cys Pro Pro Gly
230                 235                 240                 245

ttt atg gga agg acg tgt gag aag gct tgt gaa ctg cac acg ttt ggc   823
Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu Leu His Thr Phe Gly
                250                 255                 260

aga act tgt aaa gaa agg tgc agt gga caa gag gga tgc aag tct tat   871
Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu Gly Cys Lys Ser Tyr
            265                 270                 275

gtg ttc tgt ctc cct gac ccc tat ggg tgt tcc tgt gcc aca ggc tgg   919
Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser Cys Ala Thr Gly Trp
        280                 285                 290

aag ggt ctg cag tgc aat gaa ggc ata cag agg atg acc cca aag ata   967
Lys Gly Leu Gln Cys Asn Glu Gly Ile Gln Arg Met Thr Pro Lys Ile
    295                 300                 305

gtg gat ttg cca gat cat ata gaa gta aac agt ggt aaa ttt aat ccc   1015
Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
310                 315                 320                 325

att tgc aaa gct tct ggc tgg ccg cta cct act aat gaa gaa atg acc   1063
Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
                330                 335                 340

ctg gtg aag ccg gat ggg aca gtg ctc cat cca aaa gac ttt aac cat   1111
Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
            345                 350                 355

acg gat cat ttc tca gta gcc ata ttc acc atc cac cgg atc ctc ccc   1159
Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
        360                 365                 370

cct gac tca gga gtt tgg gtc tgc agt gtg aac aca gtg gct ggg atg   1207
Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
    375                 380                 385

gtg gaa aag ccc ttc aac att tct gtt aaa gtt ctt cca aag ccc ctg   1255
Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
390                 395                 400                 405

aat gcc cca aac gtg att gac act gga cat aac ttt gct gtc atc aac   1303
Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
                410                 415                 420
```

```
atc agc tct gag cct tac ttt ggg gat gga cca atc aaa tcc aag aag   1351
Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
            425                 430                 435

ctt cta tac aaa ccc gtt aat cac tat gag gct tgg caa cat att caa   1399
Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
        440                 445                 450

gta tcc atg gag aaa cag agg ctg act aaa gca aat agt gac aaa tga   1447
Val Ser Met Glu Lys Gln Arg Leu Thr Lys Ala Asn Ser Asp Lys  *
    455                 460                 465

gattgttaca ctcaactatt                                            1467

<210> 133
<211> 468
<212> PRT
<213> Homo Sapiens

<400> 133
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
```

```
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Gly Ile Gln Arg
    290                 295                 300
Met Thr Pro Lys Ile Val Asp Leu Pro Asp His Ile Glu Val Asn Ser
305                 310                 315                 320
Gly Lys Phe Asn Pro Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr
                325                 330                 335
Asn Glu Glu Met Thr Leu Val Lys Pro Asp Gly Thr Val Leu His Pro
            340                 345                 350
Lys Asp Phe Asn His Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile
        355                 360                 365
His Arg Ile Leu Pro Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn
    370                 375                 380
Thr Val Ala Gly Met Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val
385                 390                 395                 400
Leu Pro Lys Pro Leu Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn
                405                 410                 415
Phe Ala Val Ile Asn Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro
            420                 425                 430
Ile Lys Ser Lys Lys Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala
        435                 440                 445
Trp Gln His Ile Gln Val Ser Met Glu Lys Gln Arg Leu Thr Lys Ala
    450                 455                 460
Asn Ser Asp Lys
465
```

<210> 134
<211> 934
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (17)...(772)

<400> 134

```
ggtcggcctc tggagt atg gtc tgg cgg gtg ccc cct ttc ttg ctc ccc atc 52
                  Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile
                   1               5                  10

ctc ttc ttg gct tct cat gtg ggc gcg gcg gtg gac ctg acg ctg ctg   100
Leu Phe Leu Ala Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu
          15                  20                  25

gcc aac ctg cgg ctc acg gac ccc cag cgc ttc ttc ctg act tgc gtg   148
Ala Asn Leu Arg Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val
      30                  35                  40

tct ggg gag gcc ggg gcg ggg agg ggc tcg gac gcc tgg ggc ccg ccc   196
Ser Gly Glu Ala Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro
  45                  50                  55                  60

ctg ctg ctg gag aag gac gac cgt atc gtg cgc acc ccg ccc ggg cca   244
Leu Leu Leu Glu Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro
                  65                  70                  75
```

```
ccc ctg cgc ctg gcg cgc aac ggt tcg cac cag gtc acg ctt cgc ggc   292
Pro Leu Arg Leu Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly
            80                  85                  90

ttc tcc aag ccc tcg gac ctc gtg ggc gtc ttc tcc tgc gtg ggc ggt   340
Phe Ser Lys Pro Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly
        95                 100                 105

gct ggg gcg cgg cgc acg cgc gtc atc tac gtg cac aac agc cct gga   388
Ala Gly Ala Arg Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly
    110                 115                 120

gcc cac ctg ctt cca gac aag gtc aca cac act gtg aac aaa ggt gac   436
Ala His Leu Leu Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp
125                 130                 135                 140

acc gct gta ctt tct gca cgt gtg cac aag gag aag cag aca gac gtg   484
Thr Ala Val Leu Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val
                145                 150                 155

atc tgg aag agc aac gga tcc tac ttc tac acc ctg gac tgg cat gaa   532
Ile Trp Lys Ser Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu
            160                 165                 170

gcc cag gat ggg cgg ttc ctg ctg cag ctc cca aat gtg cag cca cca   580
Ala Gln Asp Gly Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro
        175                 180                 185

tcg agc ggc atc tac agt gcc act tac ctg gaa gcc agc ccc ctg ggc   628
Ser Ser Gly Ile Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly
    190                 195                 200

agc gcc ttc ttt cgg ctc atc gtg cgg ggt cag agg cag agg gca gag   676
Ser Ala Phe Phe Arg Leu Ile Val Arg Gly Gln Arg Gln Arg Ala Glu
205                 210                 215                 220

gtt gtg ggt agg gtg gga ggc tgg gag ccc tat ggg tac ttc ctg tgg   724
Val Val Gly Arg Val Gly Gly Trp Glu Pro Tyr Gly Tyr Phe Leu Trp
                225                 230                 235

gtc ccc tgg agc ccc tgg atc tcc agt cct cag tgg tca ggt ggg tga   772
Val Pro Trp Ser Pro Trp Ile Ser Ser Pro Gln Trp Ser Gly Gly  *
            240                 245                 250

gggtcagctg ctgaagacac cttcctccag gttgtggggc tgggcgctgg gggccaggct 832
gtaccaagga gtgcccaggt tgcctacatg gaggtgtctg ccacgaccat gacggcgaat 892
gtgtatgccc ccctggcttc actggcaccc gctgtgaaca gg                    934

<210> 135
<211> 251
<212> PRT
<213> Homo Sapiens

<400> 135
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
```

```
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Gln Arg Gln Arg Ala Glu Val Val Gly Arg
    210                 215                 220
Val Gly Gly Trp Glu Pro Tyr Gly Tyr Phe Leu Trp Val Pro Trp Ser
225                 230                 235                 240
Pro Trp Ile Ser Ser Pro Gln Trp Ser Gly Gly
                245                 250
```

<210> 136
<211> 1619
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (14)...(1153)

<400> 136

```
cggcctctgg agt atg gtc tgg cgg gtg ccc cct ttc ttg ctc ccc atc    49
               Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile
                1               5                   10

ctc ttc ttg gct tct cat gtg ggc gcg gcg gtg gac ctg acg ctg ctg   97
Leu Phe Leu Ala Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu
         15                  20                  25

gcc aac ctg cgg ctc acg gac ccc cag cgc ttc ttc ctg act tgc gtg   145
Ala Asn Leu Arg Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val
     30                  35                  40

tct ggg gag gcc ggg gcg ggg agg ggc tcg gac gcc tgg ggc ccg ccc   193
```

```
Ser Gly Glu Ala Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro
 45                  50                  55                  60

ctg ctg ctg gag aag gac gac cgt atc gtg cgc acc ccg ccc ggg cca   241
Leu Leu Leu Glu Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro
                65                  70                  75

ccc ctg cgc ctg gcg cgc aac ggt tcg cac cag gtc acg ctt cgc ggc   289
Pro Leu Arg Leu Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly
            80                  85                  90

ttc tcc aag ccc tcg gac ctc gtg ggc gtc ttc tcc tgc gtg ggc ggt   337
Phe Ser Lys Pro Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly
        95                  100                 105

gct ggg gcg cgg cgc acg cgc gtc atc tac gtg cac aac agc cct gga   385
Ala Gly Ala Arg Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly
    110                 115                 120

gcc cac ctg ctt cca gac aag gtc aca cac act gtg aac aaa ggt gac   433
Ala His Leu Leu Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp
125                 130                 135                 140

acc gct gta ctt tct gca cgt gtg cac aag gag aag cag aca gac gtg   481
Thr Ala Val Leu Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val
                145                 150                 155

atc tgg aag agc aac gga tcc tac ttc tac acc ctg gac tgg cat gaa   529
Ile Trp Lys Ser Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu
            160                 165                 170

gcc cag gat ggg cgg ttc ctg ctg cag ctc cca aat gtg cag cca cca   577
Ala Gln Asp Gly Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro
        175                 180                 185

tcg agc ggc atc tac agt gcc act tac ctg gaa gcc agc ccc ctg ggc   625
Ser Ser Gly Ile Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly
    190                 195                 200

agc gcc ttc ttt cgg ctc atc gtg cgg ggt tgt ggg gct ggg cgc tgg   673
Ser Ala Phe Phe Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp
205                 210                 215                 220

ggg cca ggc tgt acc aag gag tgc cca ggt tgc cta cat gga ggt gtc   721
Gly Pro Gly Cys Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val
                225                 230                 235

tgc cac gac cat gac ggc gaa tgt gta tgc ccc cct ggc ttc act ggc   769
Cys His Asp His Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly
            240                 245                 250

acc cgc tgt gaa cag gcc tgc aga gag ggc cgt ttt ggg cag agc tgc   817
Thr Arg Cys Glu Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys
        255                 260                 265

cag gag cag tgc cca ggc ata tca ggc tgc cgg ggc ctc acc ttc tgc   865
```

```
Gln Glu Gln Cys Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys
    270                 275                 280

ctc cca gac ccc tat ggc tgc tct tgt gga tct ggc tgg aga gga agc   913
Leu Pro Asp Pro Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser
285                 290                 295                 300

cag tgc caa gaa gct tgt gcc cct ggt cat ttt ggg gct gat tgc cga   961
Gln Cys Gln Glu Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg
                305                 310                 315

ctc cag tgc cag tgt cag aat ggt ggc act tgt gac cgg ttc agt ggt   1009
Leu Gln Cys Gln Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly
            320                 325                 330

tgt gtc tgc ccc tct ggg tgg cat gga gtg cac tgt gag aag tca ggc   1057
Cys Val Cys Pro Ser Gly Trp His Gly Val His Cys Glu Lys Ser Gly
        335                 340                 345

tgg agg gac tgg gta gat acc tcc act gag aaa cag aac acg gat gag   1105
Trp Arg Asp Trp Val Asp Thr Ser Thr Glu Lys Gln Asn Thr Asp Glu
    350                 355                 360

ggg cgc ttt ggt ggt cac gtg tct gcc cct gtg gga gct cca gga tga   1153
Gly Arg Phe Gly Gly His Val Ser Ala Pro Val Gly Ala Pro Gly  *
365                 370                 375

gtgtcctttc tccccagacc ggatccccca gatcctcaac atggcctcag aactggagtt 1213
caacttagag acgatgcccc ggatcaactg tgcagctgca gggaacccct tccccgtgcg 1273
gggcagcata gagctacgca agccagacgg cactgtgctc ctgtccacca aggccattgt 1333
ggagccagag aagaccacag ctgagttcga ggtgccccgc ttggttcttg cggacagtgg 1393
gttctgggag tgccgtgtgt ccacatctgg cggccaagac agccggcgct tcaaggtcaa 1453
tgtgaaagtg ccccccgtgc ccctggctgc acctcggctc ctgaccaagc agagccgcca 1513
gcttgtggtc tccccgctgg tctcgttctc tggggatgga cccatctcca ctgtccgcct 1573
gcactaccgg ccccaggaca gtaccatgga ctggtcgacc attgtg                1619

<210> 137
<211> 379
<212> PRT
<213> Homo Sapiens

<400> 137
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
```

```
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
                245                 250                 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300
Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305                 310                 315                 320
Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
                325                 330                 335
Ser Gly Trp His Gly Val His Cys Glu Lys Ser Gly Trp Arg Asp Trp
            340                 345                 350
Val Asp Thr Ser Thr Glu Lys Gln Asn Thr Asp Glu Gly Arg Phe Gly
        355                 360                 365
Gly His Val Ser Ala Pro Val Gly Ala Pro Gly
    370                 375


<210> 138
<211> 740
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (34)...(519)

<400> 138
tcgtcctggc tggcctgggt cggcctctgg agt atg gtc tgg cgg gtg ccc cct  54
                                      Met Val Trp Arg Val Pro Pro
                                       1               5

ttc ttg ctc ccc atc ctc ttc ttg gct tct cat gtg ggc gcg gcg gtg   102
Phe Leu Leu Pro Ile Leu Phe Leu Ala Ser His Val Gly Ala Ala Val
         10                  15                  20

gac ctg acg ctg ctg gcc aac ctg cgg ctc acg gac ccc cag cgc ttc   150
Asp Leu Thr Leu Leu Ala Asn Leu Arg Leu Thr Asp Pro Gln Arg Phe
```

```
     25                  30                  35

ttc ctg act tgc gtg tct ggg gag gcc ggg gcg ggg agg ggc tcg gac   198
Phe Leu Thr Cys Val Ser Gly Glu Ala Gly Ala Gly Arg Gly Ser Asp
 40                  45                  50                  55

gcc tgg ggc ccg ccc ctg ctg ctg gag aag gac gac cgt atc gtg cgc   246
Ala Trp Gly Pro Pro Leu Leu Leu Glu Lys Asp Asp Arg Ile Val Arg
                 60                  65                  70

acc ccg ccc ggg cca ccc ctg cgc ctg gcg cgc aac ggt tcg cac cag   294
Thr Pro Pro Gly Pro Pro Leu Arg Leu Ala Arg Asn Gly Ser His Gln
             75                  80                  85

gtc acg ctt cgc ggc ttc tcc aag ccc tcg gac ctc gtg ggc gtc ttc   342
Val Thr Leu Arg Gly Phe Ser Lys Pro Ser Asp Leu Val Gly Val Phe
         90                  95                 100

tcc tgc gtg ggc ggt gct ggg gcg cgg cgc acg cgc gtc atc tac gtg   390
Ser Cys Val Gly Gly Ala Gly Ala Arg Arg Thr Arg Val Ile Tyr Val
    105                 110                 115

cac aac agc cct gga ggt gag tta ggc agg cgg ggg gat ggc gcg ggg   438
His Asn Ser Pro Gly Gly Glu Leu Gly Arg Arg Gly Asp Gly Ala Gly
120                 125                 130                 135

aaa acc agg ccg ctg acc cac ctt cca ccc cgc agc cca cct gct tcc   486
Lys Thr Arg Pro Leu Thr His Leu Pro Pro Arg Ser Pro Pro Ala Ser
                140                 145                 150

aga caa ggt cac aca cac tgt gaa caa agg tga caccgctgta ctttctgcac 539
Arg Gln Gly His Thr His Cys Glu Gln Arg  *
            155                 160

gtgtgcacaa ggagaagcag acagacgtga tctggaagag caacggatcc tacttctaca 599
ccctggactg gcatgaagcc caggatgggc ggttcctgct gcagctccca aatgtgcagc 659
caccatcgag cggcatctac agtgccactt acctggaagc cagccccctg ggcagcgcct 719
tctttcggct catcgtgcgg g                                          740

<210> 139
<211> 161
<212> PRT
<213> Homo Sapiens

<400> 139
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
```

```
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Gly Glu Leu Gly
        115                 120                 125
Arg Arg Gly Asp Gly Ala Gly Lys Thr Arg Pro Leu Thr His Leu Pro
    130                 135                 140
Pro Arg Ser Pro Pro Ala Ser Arg Gln Gly His Thr His Cys Glu Gln
145                 150                 155                 160
Arg
```

<210> 140
<211> 1761
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (14)...(1258)

<400> 140

```
cggcctctgg agt atg gtc tgg cgg gtg ccc cct ttc ttg ctc ccc atc    49
               Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile
                1               5                   10

ctc ttc ttg gct tct cat gtg ggc gcg gcg gtg gac ctg acg ctg ctg   97
Leu Phe Leu Ala Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu
         15                  20                  25

gcc aac ctg cgg ctc acg gac ccc cag cgc ttc ttc ctg act tgc gtg   145
Ala Asn Leu Arg Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val
     30                  35                  40

tct ggg gag gcc ggg gcg ggg agg ggc tcg gac gcc tgg ggc ccg ccc   193
Ser Gly Glu Ala Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro
 45                  50                  55                  60

ctg ctg ctg gag aag gac gac cgt atc gtg cgc acc ccg ccc ggg cca   241
Leu Leu Leu Glu Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro
                 65                  70                  75

ccc ctg cgc ctg gcg cgc aac ggt tcg cac cag gtc acg ctt cgc ggc   289
Pro Leu Arg Leu Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly
             80                  85                  90

ttc tcc aag ccc tcg gac ctc gtg ggc gtc ttc tcc tgc gtg ggc ggt   337
Phe Ser Lys Pro Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly
         95                  100                 105

gct ggg gcg cgg cgc acg cgc gtc atc tac gtg cac aac agc cct gga   385
Ala Gly Ala Arg Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly
    110                 115                 120

gcc cac ctg ctt cca gac aag gtc aca cac act gtg aac aaa ggt gac   433
```

```
Ala His Leu Leu Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp
125                 130                 135                 140

acc gct gta ctt tct gca cgt gtg cac aag gag aag cag aca gac gtg   481
Thr Ala Val Leu Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val
                145                 150                 155

atc tgg aag agc aac gga tcc tac ttc tac acc ctg gac tgg cat gaa   529
Ile Trp Lys Ser Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu
            160                 165                 170

gcc cag gat ggg cgg ttc ctg ctg cag ctc cca aat gtg cag cca cca   577
Ala Gln Asp Gly Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro
        175                 180                 185

tcg agc ggc atc tac agt gcc act tac ctg gaa gcc agc ccc ctg ggc   625
Ser Ser Gly Ile Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly
    190                 195                 200

agc gcc ttc ttt cgg ctc atc gtg cgg ggt tgt ggg gct ggg cgc tgg   673
Ser Ala Phe Phe Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp
205                 210                 215                 220

ggg cca ggc tgt acc aag gag tgc cca ggt tgc cta cat gga ggt gtc   721
Gly Pro Gly Cys Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val
                225                 230                 235

tgc cac gac cat gac ggc gaa tgt gta tgc ccc cct ggc ttc act ggc   769
Cys His Asp His Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly
            240                 245                 250

acc cgc tgt gaa cag gcc tgc aga gag ggc cgt ttt ggg cag agc tgc   817
Thr Arg Cys Glu Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys
        255                 260                 265

cag gag cag tgc cca ggc ata tca ggc tgc cgg ggc ctc acc ttc tgc   865
Gln Glu Gln Cys Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys
    270                 275                 280

ctc cca gac ccc tat ggc tgc tct tgt gga tct ggc tgg aga gga agc   913
Leu Pro Asp Pro Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser
285                 290                 295                 300

cag tgc caa gaa gct tgt gcc cct ggt cat ttt ggg gct gat tgc cga   961
Gln Cys Gln Glu Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg
                305                 310                 315

ctc cag tgc cag tgt cag aat ggt ggc act tgt gac cgg ttc agt ggt   1009
Leu Gln Cys Gln Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly
            320                 325                 330

tgt gtc tgc ccc tct ggg tgg cat gga gtg cac tgt gag aag tca gac   1057
Cys Val Cys Pro Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp
        335                 340                 345

cgg atc ccc cag atc ctc aac atg gcc tca gaa ctg gag ttc aac tta   1105
```

```
Arg Ile Pro Gln Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu
    350                 355                 360

gag acg atg ccc cgg atc aac tgt gca gct gca ggg aac ccc ttc ccc   1153
Glu Thr Met Pro Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro
365                 370                 375                 380

gtg cgg ggc agc ata gag cta cgc aag cca gac ggc act gtg ctc ctg   1201
Val Arg Gly Ser Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu
                385                 390                 395

gtc agc ccc caa tca ccc caa ccc acc agc ccc tca ggc cgc ctg ctt   1249
Val Ser Pro Gln Ser Pro Gln Pro Thr Ser Pro Ser Gly Arg Leu Leu
            400                 405                 410

cac agc tga tccctaagac cccctagtcc ctcagaactt tctgcagggc           1298
His Ser  *


ccacccattg gcctgaccat tgctcacatg aggtcaggct gattggtgag ggggctgcca 1358
ctgggcctct gtcctgccat cagtccagac ggacacctgg gtgcctgcca cagaggtgcc 1418
cgttccctgt gacctgtccc cttcccccat ctcttttagt ccaccaaggc cattgtggag 1478
ccagagaaga ccacagctga gttcgaggtg ccccgcttgg ttcttgcgga cagtgggttc 1538
tgggagtgcc gtgtgtccac atctggcggc caagacagcc ggcgcttcaa ggtcaatgtg 1598
aaagtgcccc ccgtgccccc ggctgcacct cggctcctga ccaagcagag ccgccagctt 1658
gtggtctccc cgctggtctc gttctctggg gatggaccca tctccactgt ccgcctgcac 1718
taccggcccc aggacagtac catggactgg tcgaccattg tgg                   1761

<210> 141
<211> 414
<212> PRT
<213> Homo Sapiens

<400> 141
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
```

```
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
                245                 250                 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300
Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305                 310                 315                 320
Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
                325                 330                 335
Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp Arg Ile Pro Gln
            340                 345                 350
Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu Glu Thr Met Pro
        355                 360                 365
Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser
    370                 375                 380
Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Val Ser Pro Gln
385                 390                 395                 400
Ser Pro Gln Pro Thr Ser Pro Ser Gly Arg Leu Leu His Ser
                405                 410
```

<210> 142
<211> 1230
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (14)...(967)

<400> 142

```
cggcctctgg agt atg gtc tgg cgg gtg ccc cct ttc ttg ctc ccc atc    49
               Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile
                1               5                   10

ctc ttc ttg gct tct cat gtg ggc gcg gcg gtg gac ctg acg ctg ctg   97
Leu Phe Leu Ala Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu
         15                  20                  25

gcc aac ctg cgg ctc acg gac ccc cag cgc ttc ttc ctg act tgc gtg   145
Ala Asn Leu Arg Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val
     30                  35                  40

tct ggg gag gcc ggg gcg ggg agg ggc tcg gac gcc tgg ggc ccg ccc   193
Ser Gly Glu Ala Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro
```

```
 45                  50                  55                  60

ctg ctg ctg gag aag gac gac cgt atc gtg cgc acc ccg ccc ggg cca   241
Leu Leu Leu Glu Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro
                65                  70                  75

ccc ctg cgc ctg gcg cgc aac ggt tcg cac cag gtc acg ctt cgc ggc   289
Pro Leu Arg Leu Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly
            80                  85                  90

ttc tcc aag ccc tcg gac ctc gtg ggc gtc ttc tcc tgc gtg ggc ggt   337
Phe Ser Lys Pro Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly
        95                  100                 105

gct ggg gcg cgg cgc acg cgc gtc atc tac gtg cac aac agc cct gga   385
Ala Gly Ala Arg Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly
    110                 115                 120

gcc cac ctg ctt cca gac aag gtc aca cac act gtg aac aaa ggt gac   433
Ala His Leu Leu Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp
125                 130                 135                 140

acc gct gta ctt tct gca cgt gtg cac aag gag aag cag aca gac gtg   481
Thr Ala Val Leu Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val
                145                 150                 155

atc tgg aag agc aac gga tcc tac ttc tac acc ctg gac tgg cat gaa   529
Ile Trp Lys Ser Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu
            160                 165                 170

gcc cag gat ggg cgg ttc ctg ctg cag ctc cca aat gtg cag cca cca   577
Ala Gln Asp Gly Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro
        175                 180                 185

tcg agc ggc atc tac agt gcc act tac ctg gaa gcc agc ccc ctg ggc   625
Ser Ser Gly Ile Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly
    190                 195                 200

agc gcc ttc ttt cgg ctc atc gtg cgg ggt tgt ggg gct ggg cgc tgg   673
Ser Ala Phe Phe Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp
205                 210                 215                 220

ggg cca ggc tgt acc aag gag tgc cca ggt tgc cta cat gga ggt gtc   721
Gly Pro Gly Cys Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val
                225                 230                 235

tgc cac gac cat gac ggc gaa tgt gta tgc ccc cct ggc ttc act ggc   769
Cys His Asp His Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly
            240                 245                 250

acc cgc tgt gaa cag gcc tgc aga gag ggc cgt ttt ggg cag agc tgc   817
Thr Arg Cys Glu Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys
        255                 260                 265

cag gag cag tgc cca ggc ata tca ggc tgc cgg ggc ctc acc ttc tgc   865
Gln Glu Gln Cys Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys
```

```
    270                 275                 280

ctc cca gac ccc tat ggc tgc tct tgt gga tct ggc tgg aga gga agc   913
Leu Pro Asp Pro Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser
285                 290                 295                 300

cag tgc caa gaa gtc cac caa ggc cat tgt gga gcc aga gaa gac cac   961
Gln Cys Gln Glu Val His Gln Gly His Cys Gly Ala Arg Glu Asp His
                305                 310                 315

agc tga gttcgaggtg ccccgcttgg ttcttgcgga cagtgggttc tgggagtgcc    1017
Ser  *


gtgtgtccac atctggcggc caagacagcc ggcgcttcaa ggtcaatgtg aaagtgcccc 1077
ccgtgcccct ggctgcacct cggctcctga ccaagcagag ccgccagctt gtggtctccc 1137
cgctggtctc gttctctggg gatggaccca tctccactgt ccgcctgcac taccggcccc 1197
aggacagtac catggactgg tcgaccattg tgg                              1230

<210> 143
<211> 317
<212> PRT
<213> Homo Sapiens

<400> 143
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
```

```
                245                 250                 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300
Val His Gln Gly His Cys Gly Ala Arg Glu Asp His Ser
305                 310                 315


<210> 144
<211> 1331
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (24)...(944)

<400> 144
cctgccactt ccccaccgag gcc atg ggc cca gga gtt ctg ctg ctc ctg ctg 53
                          Met Gly Pro Gly Val Leu Leu Leu Leu Leu
                           1               5                  10

gtg gcc aca gct tgg cat ggt cag gga atc cca gtg ata gag ccc agt   101
Val Ala Thr Ala Trp His Gly Gln Gly Ile Pro Val Ile Glu Pro Ser
                15                  20                  25

gtc cct gag ctg gtc gtg aag cca gga gca acg gtg acc ttg cga tgt   149
Val Pro Glu Leu Val Val Lys Pro Gly Ala Thr Val Thr Leu Arg Cys
            30                  35                  40

gtg ggc aat ggc agc gtg gaa tgg gat ggc ccc cca tca cct cac tgg   197
Val Gly Asn Gly Ser Val Glu Trp Asp Gly Pro Pro Ser Pro His Trp
        45                  50                  55

acc ctg tac tct gat ggc tcc agc agc atc ctc agc acc aac aac gct   245
Thr Leu Tyr Ser Asp Gly Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala
    60                  65                  70

acc ttc caa aac acg ggg acc tat cgc tgc act gag cct gga gac ccc   293
Thr Phe Gln Asn Thr Gly Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro
75                  80                  85                  90

ctg gga ggc agc gcc gcc atc cac ctc tat gtc aaa gac cct gcc cgg   341
Leu Gly Gly Ser Ala Ala Ile His Leu Tyr Val Lys Asp Pro Ala Arg
                95                  100                 105

ccc tgg aac gtg cta gca cag gag gtg gtc gtg ttc gag gac cag gac   389
Pro Trp Asn Val Leu Ala Gln Glu Val Val Val Phe Glu Asp Gln Asp
            110                 115                 120

gca cta ctg ccc tgt ctg ctc aca gac ccg gtg ctg gaa gca ggc gtc   437
Ala Leu Leu Pro Cys Leu Leu Thr Asp Pro Val Leu Glu Ala Gly Val
        125                 130                 135
```

```
tcg ctg gtg cgt gtg cgt ggc cgg ccc ctc atg cgc cac acc aac tac   485
Ser Leu Val Arg Val Arg Gly Arg Pro Leu Met Arg His Thr Asn Tyr
    140                 145                 150

tcc ttc tcg ccc tgg cat ggc ttc acc atc cac agg gcc aag ttc att   533
Ser Phe Ser Pro Trp His Gly Phe Thr Ile His Arg Ala Lys Phe Ile
155                 160                 165                 170

cag agc cag gac tat caa tgc agt gcc ctg atg ggt ggc agg aag gtg   581
Gln Ser Gln Asp Tyr Gln Cys Ser Ala Leu Met Gly Gly Arg Lys Val
                175                 180                 185

atg tcc atc agc atc cgg ctg aaa gtg cag aaa gtc atc cca ggg ccc   629
Met Ser Ile Ser Ile Arg Leu Lys Val Gln Lys Val Ile Pro Gly Pro
            190                 195                 200

cca gcc ttg aca ctg gtg cct gca gag ctg gtg cgg att cga ggg gag   677
Pro Ala Leu Thr Leu Val Pro Ala Glu Leu Val Arg Ile Arg Gly Glu
        205                 210                 215

gct gcc cag atc gtg tgc tca gcc agc agc gtt gat gtt aac ttt gat   725
Ala Ala Gln Ile Val Cys Ser Ala Ser Ser Val Asp Val Asn Phe Asp
    220                 225                 230

gtc ttc ctc caa cac aac aac acc aag ctc gca atc cct caa caa tct   773
Val Phe Leu Gln His Asn Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser
235                 240                 245                 250

gac ttt cat aat aac cgt tac caa aaa gtc ctg acc ctc aac ctc gat   821
Asp Phe His Asn Asn Arg Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp
                255                 260                 265

caa gta gat ttc caa cat gcc ggc aac tac tcc tgc gtg gcc agc aac   869
Gln Val Asp Phe Gln His Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn
            270                 275                 280

gtg cag ggc aag cac tcc acc tcc atg ttc ttc cgg gtg gta ggc aca   917
Val Gln Gly Lys His Ser Thr Ser Met Phe Phe Arg Val Val Gly Thr
        285                 290                 295

cct tca ccc tct ctc tgc ccc gcc tga agccctctga ggctggccgc         964
Pro Ser Pro Ser Leu Cys Pro Ala  *
    300                 305

tactccttcc tggccagaaa cccaggaggc tggagagctc tgacgtttga gctcaccctt 1024
cgataccccc cagaggtaag cgtcatatgg acattcatca acggctctgg cacccttttg 1084
tgtgctgcct ctgggtaccc ccagcccaac gtgacatggc tgcagtgcag tggccacact 1144
gataggtgtg atgaggccca agtgctgcag gtctgggatg acccataccc tgaggtcctg 1204
agccaggagc ccttccacaa ggtgacggtg cagagcctgc tgactgttga gaccttagag 1264
cacaaccaaa cctacgagtg cagggcccac aacagcgtgg ggagtggctc ctgggccttc 1324
ataccca                                                          1331

<210> 145
<211> 306
<212> PRT
```

<213> Homo Sapiens

<400> 145

```
Met Gly Pro Gly Val Leu Leu Leu Leu Leu Val Ala Thr Ala Trp His
 1               5                  10                  15
Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
            20                  25                  30
Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
        35                  40                  45
Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
    50                  55                  60
Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65                  70                  75                  80
Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
                85                  90                  95
Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
            100                 105                 110
Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
        115                 120                 125
Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
    130                 135                 140
Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145                 150                 155                 160
Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
                165                 170                 175
Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
            180                 185                 190
Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val
        195                 200                 205
Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
    210                 215                 220
Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225                 230                 235                 240
Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
                245                 250                 255
Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
            260                 265                 270
Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
        275                 280                 285
Thr Ser Met Phe Phe Arg Val Val Gly Thr Pro Ser Pro Ser Leu Cys
    290                 295                 300
Pro Ala
305
```

<210> 146
<211> 1508
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (7)...(1017)

<400> 146

```
gacacc atg cgg ctt ccg ggt gcg atg cca gct ctg gcc ctc aaa ggc    48
```

```
       Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly
         1               5                  10

gag ctg ctg ttg ctg tct ctc ctg tta ctt ctg gaa cca cag atc tct   96
Glu Leu Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser
 15                  20                  25                  30

cag ggc ctg gtc gtc aca ccc ccg ggg cca gag ctt gtc ctc aat gtc   144
Gln Gly Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val
                 35                  40                  45

tcc agc acc ttc gtt ctg acc tgc tcg ggt tca gct ccg gtg gtg tgg   192
Ser Ser Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp
             50                  55                  60

gaa cgg atg tcc cag gag ccc cca cag gaa atg gcc aag gcc cag gat   240
Glu Arg Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp
         65                  70                  75

ggc acc ttc tcc agc gtg ctc aca ctg acc aac ctc act ggg cta gac   288
Gly Thr Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp
     80                  85                  90

acg gga gaa tac ttt tgc acc cac aat gac tcc cgt gga ctg gag acc   336
Thr Gly Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr
 95                  100                 105                 110

gat gag cgg aaa cgg ctc tac atc ttt gtg cca gat ccc acc gtg ggc   384
Asp Glu Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly
                115                 120                 125

ttc ctc cct aat gat gcc gag gaa cta ttc atc ttt ctc acg gaa ata   432
Phe Leu Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile
            130                 135                 140

act gag atc acc att cca tgc cga gta aca gac cca cag ctg gtg gtg   480
Thr Glu Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val
        145                 150                 155

aca ctg cac gag aag aaa ggg gac gtt gca ctg cct gtc ccc tat gat   528
Thr Leu His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp
    160                 165                 170

cac caa cgt ggc ttt tct ggt atc ttt gag gac aga agc tac atc tgc   576
His Gln Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys
175                 180                 185                 190

aaa acc acc att ggg gac agg gag gtg gat tct gat gcc tac tat gtc   624
Lys Thr Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val
                195                 200                 205

tac aga ctc cag gtg tca tcc atc aac gtc tct gtg aac gca gtg cag   672
Tyr Arg Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln
            210                 215                 220

act gtg gtc cgc cag ggt gag aac atc acc ctc atg tgc att gtg atc   720
```

```
Thr Val Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile
        225                 230                 235

ggg aat gag gtg gtc aac ttc gag tgg aca tac ccc cgc aaa gaa agt   768
Gly Asn Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser
    240                 245                 250

ggg cgg ctg gtg gag ccg gtg act gac ttc ctc ttg gat atg cct tac   816
Gly Arg Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr
255                 260                 265                 270

cac atc cgc tcc atc ctg cac atc ccc agt gcc gag tta gaa gac tcg   864
His Ile Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser
                275                 280                 285

ggg acc tac acc tgc aat gtg acg gag agt gtg aat gac cat cag gat   912
Gly Thr Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp
            290                 295                 300

gaa aag gcc atc aac atc acc gtg aga gcg gct acg tgc ggc tcc tgg   960
Glu Lys Ala Ile Asn Ile Thr Val Arg Ala Ala Thr Cys Gly Ser Trp
        305                 310                 315

gag agg tgg gca cac tac aat ttg ctg agc tgc atc gga gcc gga cac   1008
Glu Arg Trp Ala His Tyr Asn Leu Leu Ser Cys Ile Gly Ala Gly His
    320                 325                 330

tgc agg tag tgttcgaggc ctacccaccg cccactgtcc tgtggttcaa           1057
Cys Arg  *
335

agacaaccgc accctgggcg actccagcgc tggcgaaatc gccctgtcca cgcgcaacgt 1117
gtcggagacc cggtatgtgt cagagctgac actggttcgc gtgaaggtgg cagaggctgg 1177
ccactacacc atgcgggcct tccatgagga tgctgaggtc cagctctcct tccagctaca 1237
gatcaatgtc cctgtccgag tgctggagct aagtgagagc caccctgaca gtggggaaca 1297
gacagtccgc tgtcgtggcc ggggcatgcc ccagccgaac atcatctggt ctgcctgcag 1357
agacctcaaa aggtgtccac gtgagctgcc gcccacgctg ctggggaaca gttccgaaga 1417
ggagagccag ctggagacta acgtgacgta ctgggaggag gagcaggagt ttgaggtggt 1477
gagcacactg cgtctgcagc acgtggatcg g                                 1508

<210> 147
<211> 336
<212> PRT
<213> Homo Sapiens

<400> 147
Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
 1               5                  10                  15
Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser Gln Gly
            20                  25                  30
Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
        35                  40                  45
Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
    50                  55                  60
Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65                  70                  75                  80
```

```
Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
                85                  90                  95
Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
            100                 105                 110
Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly Phe Leu
        115                 120                 125
Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
    130                 135                 140
Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145                 150                 155                 160
His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
                165                 170                 175
Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
            180                 185                 190
Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg
        195                 200                 205
Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
    210                 215                 220
Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225                 230                 235                 240
Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
                245                 250                 255
Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
            260                 265                 270
Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
        275                 280                 285
Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
    290                 295                 300
Ala Ile Asn Ile Thr Val Arg Ala Ala Thr Cys Gly Ser Trp Glu Arg
305                 310                 315                 320
Trp Ala His Tyr Asn Leu Leu Ser Cys Ile Gly Ala Gly His Cys Arg
                325                 330                 335
```

<210> 148
<211> 1683
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (20)...(1444)

<400> 148

```
caggtcccgg cccggagct atg gag cgg cgc tgg ccc ctg ggg cta ggg ctg  52
                      Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu
                       1               5                   10

gtg ctg ctg ctc tgc gcc ccg ctg ccc ccg ggg gcg cgc gcc aag gaa  100
Val Leu Leu Leu Cys Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu
             15                  20                  25

gtt act ctg atg gac aca agc aag gca cag gga gag ctg ggc tgg ctg  148
Val Thr Leu Met Asp Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu
         30                  35                  40
```

```
ctg gat ccc cca aaa gat ggg tgg agt gaa cag caa cag ata ctg aat   196
Leu Asp Pro Pro Lys Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn
     45                  50                  55

ggg aca ccc ctg tac atg tac cag gac tgc cca atg caa gga cgc aga   244
Gly Thr Pro Leu Tyr Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg
 60                  65                  70                  75

gac act gac cac tgg ctt cgc tcc aat tgg atc tac cgc ggg gag gag   292
Asp Thr Asp His Trp Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu
                 80                  85                  90

gct tcc cgc gtc cac gtg gag ctg cag ttc acc gtg cgg gac tgc aag   340
Ala Ser Arg Val His Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys
             95                 100                 105

agt ttc cct ggg gga gcc ggg cct ctg ggc tgc aag gag acc ttc aac   388
Ser Phe Pro Gly Gly Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn
        110                 115                 120

ctt ctg tac atg gag agt gac cag gat gtg ggc att cag ctc cga cgg   436
Leu Leu Tyr Met Glu Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg
    125                 130                 135

ccc ttg ttc cag aag gta acc acg gtg gct gca gac cag agc ttc acc   484
Pro Leu Phe Gln Lys Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr
140                 145                 150                 155

att cga gac ctt gtg tct ggc tcc gtg aag ctg aat gtg gag cgc tgc   532
Ile Arg Asp Leu Val Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys
                160                 165                 170

tct ctg ggc cgc ctg acc cgc cgt ggc ctc tac ctc gct ttc cac aac   580
Ser Leu Gly Arg Leu Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn
            175                 180                 185

ccg ggt gcc tgt gtg gcc ctg gtg tct gtc cgg gtc ttc tac cag cgc   628
Pro Gly Ala Cys Val Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg
        190                 195                 200

tgt cct gag acc ctg aat ggc ttg gcc caa ttc cca gac act ctg cct   676
Cys Pro Glu Thr Leu Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro
    205                 210                 215

ggc ccc gct ggg ttg gtg gaa gtg gcg ggg acc tgc ttg ccc cac gcg   724
Gly Pro Ala Gly Leu Val Glu Val Ala Gly Thr Cys Leu Pro His Ala
220                 225                 230                 235

cgg gcc agc ccc agg ccc tca ggt gca ccc cgc atg cac tgc agc cct   772
Arg Ala Ser Pro Arg Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro
                240                 245                 250

gat ggc gag tgg ctg gtg cct gta gga cgg tgc cac tgt gag cct ggc   820
Asp Gly Glu Trp Leu Val Pro Val Gly Arg Cys His Cys Glu Pro Gly
            255                 260                 265
```

```
tat gag gaa ggt ggc agt ggc gaa gca tgt gtt gcc tgc cct agc ggc   868
Tyr Glu Glu Gly Gly Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly
        270                 275                 280

tcc tac cgg atg gac atg gac aca ccc cat tgt ctc acg tgc ccc cag   916
Ser Tyr Arg Met Asp Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln
    285                 290                 295

cag agc act gct gag tct gag ggg gcc acc atc tgt acc tgt gag agc   964
Gln Ser Thr Ala Glu Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser
300                 305                 310                 315

ggc cat tac aga gct ccc ggg gag ggc ccc cag gtg gca tgc aca ggt   1012
Gly His Tyr Arg Ala Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly
                320                 325                 330

ccc ccc tcg gcc ccc cga aac ctg agc ttc tct gcc tca ggg act cag   1060
Pro Pro Ser Ala Pro Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln
            335                 340                 345

ctc tcc ctg cgt tgg gaa ccc cca gca gat acg ggg gga cgc cag gat   1108
Leu Ser Leu Arg Trp Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp
        350                 355                 360

gtc aga tac agt gtg agg tgt tcc cag tgt cag ggc aca gca cag gac   1156
Val Arg Tyr Ser Val Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp
    365                 370                 375

ggg ggg ccc tgc cag ccc tgt ggg gtg ggc gtg cac ttc tcg ccg ggg   1204
Gly Gly Pro Cys Gln Pro Cys Gly Val Gly Val His Phe Ser Pro Gly
380                 385                 390                 395

gcc cgg ggg ctc acc aca cct gca gtg cat gtc aat ggc ctt gaa cct   1252
Ala Arg Gly Leu Thr Thr Pro Ala Val His Val Asn Gly Leu Glu Pro
                400                 405                 410

tat gcc aac tac acc ttt aat gtg gaa gcc caa aat gga gtg tca ggg   1300
Tyr Ala Asn Tyr Thr Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly
            415                 420                 425

ctg ggc agc tct ggc cat gcc agc acc tca gtc agc atc agc atg ggg   1348
Leu Gly Ser Ser Gly His Ala Ser Thr Ser Val Ser Ile Ser Met Gly
        430                 435                 440

cat gca ggt gag agg ctg aga ggg gct ggg aca ggg acc tgg tgg aga   1396
His Ala Gly Glu Arg Leu Arg Gly Ala Gly Thr Gly Thr Trp Trp Arg
    445                 450                 455

cag aag ggc tta aga cca cag aac aaa ctg atg ggc agg aag cca tag   1444
Gln Lys Gly Leu Arg Pro Gln Asn Lys Leu Met Gly Arg Lys Pro  *
460                 465                 470

aaaagttact aaggttattt ccttttttcct tacatatcca accttatccc tctggacccc 1504
cagagtcact gtcaggcctg tctctgagac tggtgaagaa agaaccgagg caactagagc 1564
tgacctgggc ggggtcccgg ccccgaagcc ctggggcgaa cctgacctat gagctgcacg 1624
tgctgaacca ggatgaagaa cggtaccaga tggttctaga acccagggtc ttgctgaca  1683
```

<210> 149
<211> 474
<212> PRT
<213> Homo Sapiens

<400> 149
Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
1 5 10 15
Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
20 25 30
Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
35 40 45
Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
50 55 60
Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65 70 75 80
Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His
85 90 95
Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
100 105 110
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
115 120 125
Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
130 135 140
Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Val
145 150 155 160
Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
165 170 175
Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
180 185 190
Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
195 200 205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
210 215 220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225 230 235 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
245 250 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
260 265 270
Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
275 280 285
Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
290 295 300
Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305 310 315 320
Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
325 330 335
Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
340 345 350
Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
355 360 365
Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
370 375 380
Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Gly Leu Thr

```
385                 390                 395                 400
Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
                405                 410                 415
Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
            420                 425                 430
His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Gly Glu Arg
        435                 440                 445
Leu Arg Gly Ala Gly Thr Gly Thr Trp Trp Arg Gln Lys Gly Leu Arg
    450                 455                 460
Pro Gln Asn Lys Leu Met Gly Arg Lys Pro
465                 470
```

<210> 150
<211> 1375
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (20)...(955)

<400> 150

```
caggtcccgg cccggagct atg gag cgg cgc tgg ccc ctg ggg cta ggg ctg  52
                       Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu
                        1               5                   10

gtg ctg ctg ctc tgc gcc ccg ctg ccc ccg ggg gcg cgc gcc aag gaa  100
Val Leu Leu Leu Cys Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu
             15                  20                  25

gtt act ctg atg gac aca agc aag gca cag gga gag ctg ggc tgg ctg  148
Val Thr Leu Met Asp Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu
         30                  35                  40

ctg gat ccc cca aaa gat ggg tgg agt gaa cag caa cag ata ctg aat  196
Leu Asp Pro Pro Lys Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn
     45                  50                  55

ggg aca ccc ctg tac atg tac cag gac tgc cca atg caa gga cgc aga  244
Gly Thr Pro Leu Tyr Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg
 60                  65                  70                  75

gac act gac cac tgg ctt cgc tcc aat tgg atc tac cgc ggg gag gag  292
Asp Thr Asp His Trp Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu
                 80                  85                  90

gct tcc cgc gtc cac gtg gag ctg cag ttc acc gtg cgg gac tgc aag  340
Ala Ser Arg Val His Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys
             95                  100                 105

agt ttc cct ggg gga gcc ggg cct ctg ggc tgc aag gag acc ttc aac  388
Ser Phe Pro Gly Gly Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn
        110                 115                 120

ctt ctg tac atg gag agt gac cag gat gtg ggc att cag ctc cga cgg  436
```

```
Leu Leu Tyr Met Glu Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg
    125                 130                 135

ccc ttg ttc cag aag gta acc acg gtg gct gca gac cag agc ttc acc   484
Pro Leu Phe Gln Lys Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr
140                 145                 150                 155

att cga gac ctt gtg tct ggc tcc gtg aag ctg aat gtg gag cgc tgc   532
Ile Arg Asp Leu Val Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys
                160                 165                 170

tct ctg ggc cgc ctg acc cgc cgt ggc ctc tac ctc gct ttc cac aac   580
Ser Leu Gly Arg Leu Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn
            175                 180                 185

ccg ggt gcc tgt gtg gcc ctg gtg tct gtc cgg gtc ttc tac cag cgc   628
Pro Gly Ala Cys Val Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg
        190                 195                 200

tgt cct gag acc ctg aat ggc ttg gcc caa ttc cca gac act ctg cct   676
Cys Pro Glu Thr Leu Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro
    205                 210                 215

ggc ccc gct ggg ttg gtg gaa gtg gcg ggg acc tgc ttg ccc cac gcg   724
Gly Pro Ala Gly Leu Val Glu Val Ala Gly Thr Cys Leu Pro His Ala
220                 225                 230                 235

cgg gcc agc ccc agg ccc tca ggt gca ccc cgc atg cac tgc agc cct   772
Arg Ala Ser Pro Arg Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro
                240                 245                 250

gat ggc gag tgg ctg gtg cct gta gga cgg tgc cac tgt gag cct ggc   820
Asp Gly Glu Trp Leu Val Pro Val Gly Arg Cys His Cys Glu Pro Gly
            255                 260                 265

tat gag gaa ggt ggc agt ggc gaa gca tgt gtt ggt aag aac gga ggc   868
Tyr Glu Glu Gly Gly Ser Gly Glu Ala Cys Val Gly Lys Asn Gly Gly
        270                 275                 280

ggt gag aac ctg agg aac cac tcg gga gga ttg cag gag tac ccc ggc   916
Gly Glu Asn Leu Arg Asn His Ser Gly Gly Leu Gln Glu Tyr Pro Gly
    285                 290                 295

aga gaa gga ggc cag tgc tcc gcc tca gtg ggt ttt taa cctgagtgtc    965
Arg Glu Gly Gly Gln Cys Ser Ala Ser Val Gly Phe  *
300                 305                 310

ccagagcagc ggacacacac atgcagagat gtttccagta gaagggattg gggcaggaag 1025
gggtggtggt ggttctgcct gtaaaaacat ttacagaacc actgctctgc tgcgttctct 1085
ctccagcctg ccctagcggc tcctaccgga tggacatgga cacaccccat tgtctcacgt 1145
gcccccagca gagcactgct gagtctgagg gggccaccat ctgtacctgt gagagcggcc 1205
attacagagc tcccggggag ggcccccagg tggcatgcac agagtcactg tcaggcctgt 1265
ctctgagact ggtgaagaaa gaaccgaggc aactagagct gacctgggcg gggtcccggc 1325
cccgaagccc tggggcgaac ctgacctatg agctgcacgt gctgaaccag            1375

<210> 151
```

<211> 311
<212> PRT
<213> Homo Sapiens

<400> 151
Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
1 5 10 15
Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
20 25 30
Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
35 40 45
Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
50 55 60
Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65 70 75 80
Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His
85 90 95
Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
100 105 110
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
115 120 125
Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
130 135 140
Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Val
145 150 155 160
Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
165 170 175
Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
180 185 190
Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
195 200 205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
210 215 220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225 230 235 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
245 250 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
260 265 270
Ser Gly Glu Ala Cys Val Gly Lys Asn Gly Gly Gly Glu Asn Leu Arg
275 280 285
Asn His Ser Gly Gly Leu Gln Glu Tyr Pro Gly Arg Glu Gly Gly Gln
290 295 300
Cys Ser Ala Ser Val Gly Phe
305 310

<210> 152
<211> 1511
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (20)...(1492)

<400> 152

```
caggtcccgg cccggagct atg gag cgg cgc tgg ccc ctg ggg cta ggg ctg  52
                      Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu
                       1               5                  10

gtg ctg ctg ctc tgc gcc ccg ctg ccc ccg ggg gcg cgc gcc aag gaa  100
Val Leu Leu Leu Cys Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu
             15                  20                  25

gtt act ctg atg gac aca agc aag gca cag gga gag ctg ggc tgg ctg  148
Val Thr Leu Met Asp Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu
         30                  35                  40

ctg gat ccc cca aaa gat ggg tgg agt gaa cag caa cag ata ctg aat  196
Leu Asp Pro Pro Lys Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn
     45                  50                  55

ggg aca ccc ctg tac atg tac cag gac tgc cca atg caa gga cgc aga  244
Gly Thr Pro Leu Tyr Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg
 60                  65                  70                  75

gac act gac cac tgg ctt cgc tcc aat tgg atc tac cgc ggg gag gag  292
Asp Thr Asp His Trp Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu
                 80                  85                  90

gct tcc cgc gtc cac gtg gag ctg cag ttc acc gtg cgg gac tgc aag  340
Ala Ser Arg Val His Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys
             95                  100                 105

agt ttc cct ggg gga gcc ggg cct ctg ggc tgc aag gag acc ttc aac  388
Ser Phe Pro Gly Gly Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn
        110                 115                 120

ctt ctg tac atg gag agt gac cag gat gtg ggc att cag ctc cga cgg  436
Leu Leu Tyr Met Glu Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg
    125                 130                 135

ccc ttg ttc cag aag gta acc acg gtg gct gca gac cag agc ttc acc  484
Pro Leu Phe Gln Lys Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr
140                 145                 150                 155

att cga gac ctt gtg tct ggc tcc gtg aag ctg aat gtg gag cgc tgc  532
Ile Arg Asp Leu Val Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys
                160                 165                 170

tct ctg ggc cgc ctg acc cgc cgt ggc ctc tac ctc gct ttc cac aac  580
Ser Leu Gly Arg Leu Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn
            175                 180                 185

ccg ggt gcc tgt gtg gcc ctg gtg tct gtc cgg gtc ttc tac cag cgc  628
Pro Gly Ala Cys Val Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg
        190                 195                 200

tgt cct gag acc ctg aat ggc ttg gcc caa ttc cca gac act ctg cct  676
Cys Pro Glu Thr Leu Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro
    205                 210                 215
```

```
ggc ccc gct ggg ttg gtg gaa gtg gcg ggg acc tgc ttg ccc cac gcg   724
Gly Pro Ala Gly Leu Val Glu Val Ala Gly Thr Cys Leu Pro His Ala
220                 225                 230                 235

cgg gcc agc ccc agg ccc tca ggt gca ccc cgc atg cac tgc agc cct   772
Arg Ala Ser Pro Arg Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro
                240                 245                 250

gat ggc gag tgg ctg gtg cct gta gga cgg tgc cac tgt gag cct ggc   820
Asp Gly Glu Trp Leu Val Pro Val Gly Arg Cys His Cys Glu Pro Gly
            255                 260                 265

tat gag gaa ggt ggc agt ggc gaa gca tgt gtt gcc tgc cct agc ggc   868
Tyr Glu Glu Gly Gly Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly
        270                 275                 280

tcc tac cgg atg gac atg gac aca ccc cat tgt ctc acg tgc ccc cag   916
Ser Tyr Arg Met Asp Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln
    285                 290                 295

cag agc act gct gag tct gag ggg gcc acc atc tgt acc tgt gag agc   964
Gln Ser Thr Ala Glu Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser
300                 305                 310                 315

ggc cat tac aga gct ccc ggg gag ggc ccc cag gtg gca tgc aca ggt   1012
Gly His Tyr Arg Ala Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly
                320                 325                 330

ccc ccc tcg gcc ccc cga aac ctg agc ttc tct gcc tca ggg act cag   1060
Pro Pro Ser Ala Pro Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln
            335                 340                 345

ctc tcc ctg cgt tgg gaa ccc cca gca gat acg ggg gga cgc cag gat   1108
Leu Ser Leu Arg Trp Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp
        350                 355                 360

gtc aga tac agt gtg agg tgt tcc cag tgt cag ggc aca gca cag gac   1156
Val Arg Tyr Ser Val Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp
    365                 370                 375

ggg ggg ccc tgc cag ccc tgt ggg gtg ggc gtg cac ttc tcg ccg ggg   1204
Gly Gly Pro Cys Gln Pro Cys Gly Val Gly Val His Phe Ser Pro Gly
380                 385                 390                 395

gcc cgg ggg ctc acc aca cct gca gtg cat gtc aat ggc ctt gaa cct   1252
Ala Arg Gly Leu Thr Thr Pro Ala Val His Val Asn Gly Leu Glu Pro
                400                 405                 410

tat gcc aac tac acc ttt aat gtg gaa gcc caa aat gga gtg tca ggg   1300
Tyr Ala Asn Tyr Thr Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly
            415                 420                 425

ctg ggc agc tct ggc cat gcc agc acc tca gtc agc atc agc atg ggg   1348
Leu Gly Ser Ser Gly His Ala Ser Thr Ser Val Ser Ile Ser Met Gly
        430                 435                 440
```

```
cat gca gat cca acc tta tcc ctc tgg acc ccc aga gtc act gtc agg   1396
His Ala Asp Pro Thr Leu Ser Leu Trp Thr Pro Arg Val Thr Val Arg
    445                 450                 455

cct gtc tct gag act ggt gaa gaa aga acc gag gca act aga gct gac   1444
Pro Val Ser Glu Thr Gly Glu Glu Arg Thr Glu Ala Thr Arg Ala Asp
460                 465                 470                 475

ctg ggc ggg gtc ccg gcc ccg aag ccc tgg ggc gaa cct gac cta tga   1492
Leu Gly Gly Val Pro Ala Pro Lys Pro Trp Gly Glu Pro Asp Leu  *
                480                 485                 490

gctgcacgtg ctgaaccag                                              1511
```

<210> 153
<211> 490
<212> PRT
<213> Homo Sapiens

<400> 153

```
Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
 1               5                  10                  15
Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
            20                  25                  30
Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
        35                  40                  45
Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
    50                  55                  60
Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65                  70                  75                  80
Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His
                85                  90                  95
Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
            100                 105                 110
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
        115                 120                 125
Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
    130                 135                 140
Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Val
145                 150                 155                 160
Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
                165                 170                 175
Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
            180                 185                 190
Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
        195                 200                 205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
    210                 215                 220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225                 230                 235                 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
                245                 250                 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
            260                 265                 270
Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
```

```
        275                 280                 285
Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
    290                 295                 300
Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305                 310                 315                 320
Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
                325                 330                 335
Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
            340                 345                 350
Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
        355                 360                 365
Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
    370                 375                 380
Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Gly Leu Thr
385                 390                 395                 400
Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
                405                 410                 415
Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
            420                 425                 430
His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Asp Pro Thr
        435                 440                 445
Leu Ser Leu Trp Thr Pro Arg Val Thr Val Arg Pro Val Ser Glu Thr
    450                 455                 460
Gly Glu Glu Arg Thr Glu Ala Thr Arg Ala Asp Leu Gly Gly Val Pro
465                 470                 475                 480
Ala Pro Lys Pro Trp Gly Glu Pro Asp Leu
                485                 490
```

<210> 154
<211> 1107
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (20)...(748)

<400> 154

```
tgcgggccgt cggccggcg atg gcc ctg gat tat cta cta ctg ctc ctc ctg  52
                      Met Ala Leu Asp Tyr Leu Leu Leu Leu Leu Leu
                       1               5                   10

gca tcc gca gtg gct gcg atg gaa gaa acg tta atg gac acc aga acg   100
Ala Ser Ala Val Ala Ala Met Glu Glu Thr Leu Met Asp Thr Arg Thr
             15                  20                  25

gct act gca gag ctg ggc tgg acg gcc aat cct gcg tcc ggg tgg gaa   148
Ala Thr Ala Glu Leu Gly Trp Thr Ala Asn Pro Ala Ser Gly Trp Glu
         30                  35                  40

gaa gtc agt ggc tac gat gaa aac ctg aac acc atc cgc acc tac cag   196
Glu Val Ser Gly Tyr Asp Glu Asn Leu Asn Thr Ile Arg Thr Tyr Gln
     45                  50                  55

gtg tgc aat gtc ttc gag ccc aac cag aac aat tgg ctg ctc acc acc   244
```

```
Val Cys Asn Val Phe Glu Pro Asn Gln Asn Asn Trp Leu Leu Thr Thr
 60                  65                  70                  75

ttc atc aac cgg cgg ggg gcc cat cgc atc tac aca gag atg cgc ttc   292
Phe Ile Asn Arg Arg Gly Ala His Arg Ile Tyr Thr Glu Met Arg Phe
                80                  85                  90

act gtg aga gac tgc agc agc ctc cct aat gtc cca gga tcc tgc aag   340
Thr Val Arg Asp Cys Ser Ser Leu Pro Asn Val Pro Gly Ser Cys Lys
            95                  100                 105

gag acc ttc aac ttg tat tac tat gag act gac tct gtc att gcc acc   388
Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Thr Asp Ser Val Ile Ala Thr
        110                 115                 120

aag aag tca gcc ttc tgg tct gag gcc ccc tac ctc aaa gta gac acc   436
Lys Lys Ser Ala Phe Trp Ser Glu Ala Pro Tyr Leu Lys Val Asp Thr
    125                 130                 135

att gct gca gat gag agc ttc tcc cag gtg gac ttt ggg gga agg ctg   484
Ile Ala Ala Asp Glu Ser Phe Ser Gln Val Asp Phe Gly Gly Arg Leu
140                 145                 150                 155

atg aag ctt gcc ctg cag gga cat tca agg cca gcc agg aag ctg aag   532
Met Lys Leu Ala Leu Gln Gly His Ser Arg Pro Ala Arg Lys Leu Lys
                160                 165                 170

gct gct ccc act gcc cct cca aca gcc gct ccc ctg cag agg cgt ctc   580
Ala Ala Pro Thr Ala Pro Pro Thr Ala Ala Pro Leu Gln Arg Arg Leu
            175                 180                 185

cca tct gca cct gtc gga ccg gtt att acc gag cgg act ttg acc ctc   628
Pro Ser Ala Pro Val Gly Pro Val Ile Thr Glu Arg Thr Leu Thr Leu
        190                 195                 200

cag aag tgg cat gca cta gcg tcc cat cag gtc ccc gca atg tta tct   676
Gln Lys Trp His Ala Leu Ala Ser His Gln Val Pro Ala Met Leu Ser
    205                 210                 215

cca tcg tca atg aga cgt cca tca ttc tgg agt ggc acc ctc caa ggg   724
Pro Ser Ser Met Arg Arg Pro Ser Phe Trp Ser Gly Thr Leu Gln Gly
220                 225                 230                 235

aga cag gtg ggc ggg atg atg tga cctacaacat catctgcaaa aagtgccggg  778
Arg Gln Val Gly Gly Met Met  *
                240

cagaccgccg gagctgctcc cgctgtgacg acaatgtgga gtttgtgccc aggcagctgg 838
gcctgacgga gtgccgcgtc tccatcagca gcctgtgggc ccacaccccc tacacctttg 898
acatccaggc catcaatgga gtctccagca agagtccctt ccccccacag cacgtctctg 958
tcaacatcac cacaaaccaa gccgcccccc ccaccgttcc catcatgcac caagtcagtg 1018
ccactatgag gagcatcacc ttgtcatggc cacagccgga gcagcccaat ggcatcatcc 1078
tggactatga gatccggtac tatgagaag                                   1107

<210> 155
<211> 242
```

<212> PRT
<213> Homo Sapiens

<400> 155
Met Ala Leu Asp Tyr Leu Leu Leu Leu Leu Leu Ala Ser Ala Val Ala
1 5 10 15
Ala Met Glu Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu
20 25 30
Gly Trp Thr Ala Asn Pro Ala Ser Gly Trp Glu Glu Val Ser Gly Tyr
35 40 45
Asp Glu Asn Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe
50 55 60
Glu Pro Asn Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg
65 70 75 80
Gly Ala His Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys
85 90 95
Ser Ser Leu Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu
100 105 110
Tyr Tyr Tyr Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe
115 120 125
Trp Ser Glu Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu
130 135 140
Ser Phe Ser Gln Val Asp Phe Gly Gly Arg Leu Met Lys Leu Ala Leu
145 150 155 160
Gln Gly His Ser Arg Pro Ala Arg Lys Leu Lys Ala Ala Pro Thr Ala
165 170 175
Pro Pro Thr Ala Ala Pro Leu Gln Arg Arg Leu Pro Ser Ala Pro Val
180 185 190
Gly Pro Val Ile Thr Glu Arg Thr Leu Thr Leu Gln Lys Trp His Ala
195 200 205
Leu Ala Ser His Gln Val Pro Ala Met Leu Ser Pro Ser Ser Met Arg
210 215 220
Arg Pro Ser Phe Trp Ser Gly Thr Leu Gln Gly Arg Gln Val Gly Gly
225 230 235 240
Met Met

<210> 156
<211> 3952
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM013993
<309> 2004-10-28

<400> 156
ggcttaggaa gtattaactg atctctgccc tagttctcat gtgttaaata tggatagtaa 60
tagtatctac cttatgaagt gactgtgaag ataaaattat ggattctgtt taagggttta 120
ggccagtgtc tggcacaggg gaagcattct aaaaatatag ctgatgctgt taaacaatga 180
ctgttgttgt tgttttactg ttattatccc caaagcggcc cattctgtct gttgctgtca 240
gctatgactc agtcccctga ttaacttacg caccacccat tttatcccct gcagagatgc 300
tgcccccacc cccttaggcc cgagggatca ggagctatgg gaccagaggc cctgtcatct 360
ttactgctgc tgctcttggt ggcaagtgga gatgctgaca tgaagggaca ttttgatcct 420
gccaagtgcc gctatgccct gggcatgcag gaccggacca tcccagacag tgacatctct 480

gcttccagct cctggtcaga ttccactgcc gcccgccaca gcaggttgga gagcagtgac 540
ggggatgggg cctggtgccc cgcagggtcg gtgtttccca aggaggagga gtacttgcag 600
gtggatctac aacgactgca cctggtggct ctggtgggca cccagggacg gcatgccggg 660
ggcctgggca aggagttctc ccggagctac cggctgcgtt actcccggga tggtcgccgc 720
tggatgggct ggaaggaccg ctggggtcag gaggtgatct caggcaatga ggaccctgag 780
ggagtggtgc tgaaggacct tgggcccccc atggttgccc gactggttcg cttctacccc 840
cgggctgacc gggtcatgag cgtctgtctg cgggtagagc tctatggctg cctctggagg 900
gatggactcc tgtcttacac cgcccctgtg gggcagacaa tgtatttatc tgaggccgtg 960
tacctcaacg actccaccta tgacggacat accgtgggcg gactgcagta tgggggtctg 1020
ggccagctgg cagatggtgt ggtggggctg gatgacttta ggaagagtca ggagctgcgg 1080
gtctggccag gctatgacta tgtgggatgg agcaaccaca gcttctccag tggctatgtg 1140
gagatggagt ttgagtttga ccggctgagg gccttccagg ctatgcaggt ccactgtaac 1200
aacatgcaca cgctgggagc ccgtctgcct ggcggggtgg aatgtcgctt ccggcgtggc 1260
cctgccatgg cctgggaggg ggagcccatg cgccacaacc taggggggcaa cctgggggac 1320
cccagagccc gggctgtctc agtgcccctt ggcggccgtg tggctcgctt tctgcagtgc 1380
cgcttcctct ttgcggggcc ctggttactc ttcagcgaaa tctccttcat ctctgatgtg 1440
gtgaacaatt cctctccggc actgggaggc accttcccgc cagccccctg gtggccgcct 1500
ggcccacctc ccaccaactt cagcagcttg gagctggagc ccagaggcca gcagcccgtg 1560
gccaaggccg aggggagccc gaccgccatc ctcatcggct gcctggtggc catcatcctg 1620
ctcctgctgc tcatcattgc cctcatgctc tggcggctgc actggcgcag gctcctcagc 1680
aaggctgaac ggagggtgtt ggaagaggag ctgacggttc acctctctgt ccctggggac 1740
actatcctca tcaacaaccg cccaggtcct agagagccac ccccgtacca ggagccccgg 1800
cctcgtggga atccgcccca ctccgctccc tgtgtcccca atggctctgc gttgctgctc 1860
tccaatccag cctaccgcct ccttctggcc acttacgccc gtccccctcg aggcccgggc 1920
ccccccacac ccgcctgggc caaacccacc aacacccagg cctacagtgg ggactatatg 1980
gagcctgaga agccaggcgc cccgcttctg cccccacctc cccagaacag cgtccccccat 2040
tatgccgagg ctgacattgt taccctgcag ggcgtcaccg ggggcaacac ctatgctgtg 2100
cctgcactgc ccccaggggc agtcggggat gggccccccа gagtggattt ccctcgatct 2160
cgactccgct tcaaggagaa gcttggcgag ggccagtttg gggaggtgca cctgtgtgag 2220
gtcgacagcc ctcaagatct ggttagtctt gatttccccc ttaatgtgcg taagggacac 2280
cctttgctgg tagctgtcaa gatcttacgg ccagatgcca ccaagaatgc caggaatgat 2340
ttcctgaaag aggtgaagat catgtcgagg ctcaaggacc caaacatcat tcggctgctg 2400
ggcgtgtgtg tgcaggacga ccccctctgc atgattactg actacatgga gaacggcgac 2460
ctcaaccagt tcctcagtgc ccaccagctg gaggacaagg cagccgaggg ggcccctggg 2520
gacgggcagg ctgcgcaggg gcccaccatc agctacccaa tgctgctgca tgtggcagcc 2580
cagatcgcct ccggcatgcg ctatctggcc acactcaact ttgtacatcg ggacctggcc 2640
acgcggaact gcctagttgg ggaaaatttc accatcaaaa tcgcagactt tggcatgagc 2700
cggaacctct atgctgggga ctattaccgt gtgcagggcc gggcagtgct gcccatccgc 2760
tggatggcct gggagtgcat cctcatgggg aagttcacga ctgcgagtga cgtgtgggcc 2820
tttggtgtga ccctgtggga ggtgctgatg ctctgtaggg cccagccctt tgggtcagct 2880
caccgacgag caggtcatcg agaacgcggg ggagttcttc cgggaccagg gccggcagtg 2940
tacctgtccc ggccgcctgc ctgcccgcag ggcctatatg agctgatgct tcggtgctgg 3000
agccgggagt ctgagcagcg accacccttt tcccagctgc atcggttcct ggcagaggat 3060
gcactcaaca cggtgtgaat cacacatcca gctgcccctc cctcagggag cgatccaggg 3120
gaagccagtg acactaaaac aagaggacac aatggcacct ctgcccttcc cctcccgaca 3180
gcccatcacc tctaatagag gcagtgagac tgcaggtggg ctgggcccac ccagggagct 3240
gatgcccctt ctccccttcc tggacacact ctcatgtccc cttcctgttc ttccttccta 3300
gaagcccccc tgtcgcccac ccagctggtc ctgtggatgg gatcctctcc accctcctct 3360
agccatccct tggggaaggg tggggagaaa tataggatag acactggaca tggcccattg 3420
gagcacctgg gccccactgg acaacactga ttcctggaga ggtggctgcg cccccagctt 3480
ctctctccct gtcacacact ggaccccact ggctgagaat ctgggggtga ggaggacaag 3540
aaggagagga aaatgtttcc ttgtgcctgc tcctgtactt gtcctcagct tgggcttctt 3600
cctcctccat cacctgaaac actggacctg ggggtagccc cgccccagcc ctcagtcacc 3660
cccacttccc acttgcagtc ttgtagctag aacttctcta agcctatacg tttctgtgga 3720
gtaaatattg ggattggggg gaaagaggga gcaacggccc atagccttgg ggttggacat 3780
ctctagtgta gctgccacat tgatttttct ataatcactt ggggtttgta cattttggg 3840

gggagagaca cagattttta cactaatata tggacctagc ttgaggcaat tttaatcccc 3900
tgcactaggc aggtaataat aaaggttgag ttttccacaa aaaaaaaaaa aa 3952

<210> 157
<211> 5777
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM002019
<309> 2004-10-28

<400> 157
gcggacactc ctctcggctc ctccccggca gcggcggcgg ctcggagcgg gctccggggc 60
tcgggtgcag cggccagcgg gcctggcggc gaggattacc cggggaagtg gttgtctcct 120
ggctggagcc gcgagacggg cgctcagggc gcggggccgg cggcggcgaa cgagaggacg 180
gactctggcg gccgggtcgt tggccggggg agcgcgggca ccgggcgagc aggccgcgtc 240
gcgctcacca tggtcagcta ctgggacacc ggggtcctgc tgtgcgcgct gctcagctgt 300
ctgcttctca caggatctag ttcaggttca aaattaaaag atcctgaact gagtttaaaa 360
ggcacccagc acatcatgca agcaggccag acactgcatc tccaatgcag gggggaagca 420
gcccataaat ggtctttgcc tgaaatggtg agtaaggaaa gcgaaaggct gagcataact 480
aaatctgcct gtggaagaaa tggcaaacaa ttctgcagta ctttaacctt gaacacagct 540
caagcaaacc acactggctt ctacagctgc aaatatctag ctgtacctac ttcaaagaag 600
aaggaaacag aatctgcaat ctatatattt attagtgata caggtagacc tttcgtagag 660
atgtacagtg aaatccccga aattatacac atgactgaag gaaggggagct cgtcattccc 720
tgccgggtta cgtcacctaa catcactgtt actttaaaaa agtttccact tgacactttg 780
atccctgatg gaaaacgcat aatctgggac agtagaaagg gcttcatcat atcaaatgca 840
acgtacaaag aaatagggct tctgacctgt gaagcaacag tcaatgggca tttgtataag 900
acaaactatc tcacacatcg acaaaccaat acaatcatag atgtccaaat aagcacacca 960
cgcccagtca aattacttag aggccatact cttgtcctca attgtactgc taccactccc 1020
ttgaacacga gagttcaaat gacctggagt taccctgatg aaaaaaataa gagagcttcc 1080
gtaaggcgac gaattgacca aagcaattcc catgccaaca tattctacag tgttcttact 1140
attgacaaaa tgcagaacaa agacaaagga ctttatactt gtcgtgtaag gagtggacca 1200
tcattcaaat ctgttaacac ctcagtgcat atatatgata aagcattcat cactgtgaaa 1260
catcgaaaac agcaggtgct tgaaaccgta gctggcaagc ggtcttaccg gctctctatg 1320
aaagtgaagg catttccctc gccggaagtt gtatggttaa aagatgggtt acctgcgact 1380
gagaaatctg ctcgctattt gactcgtggc tactcgttaa ttatcaagga cgtaactgaa 1440
gaggatgcag ggaattatac aatcttgctg agcataaaac agtcaaatgt gtttaaaaac 1500
ctcactgcca ctctaattgt caatgtgaaa ccccagattt acgaaaaggc cgtgtcatcg 1560
tttccagacc cggctctcta cccactgggc agcagacaaa tcctgacttg taccgcatat 1620
ggtatccctc aacctacaat caagtggttc tggcacccct gtaaccataa tcattccgaa 1680
gcaaggtgtg acttttgttc caataatgaa gagtccttta tcctggatgc tgacagcaac 1740
atgggaaaca gaattgagag catcactcag cgcatggcaa taatagaagg aaagaataag 1800
atggctagca ccttggttgt ggctgactct agaatttctg gaatctacat ttgcatagct 1860
tccaataaag ttgggactgt gggaagaaac ataagctttt atatcacaga tgtgccaaat 1920
gggtttcatg ttaacttgga aaaaatgccg acggaaggag aggacctgaa actgtcttgc 1980
acagttaaca agttcttata cagagacgtt acttggattt tactgcggac agttaataac 2040
agaacaatgc actacagtat tagcaagcaa aaaatggcca tcactaagga gcactccatc 2100
actcttaatc ttaccatcat gaatgtttcc ctgcaagatt caggcaccta tgcctgcaga 2160
gccaggaatg tatacacagg ggaagaaatc ctccagaaga aagaaattac aatcagagat 2220
caggaagcac catacctcct gcgaaacctc agtgatcaca cagtggccat cagcagttcc 2280
accactttag actgtcatgc taatggtgtc cccgagcctc agatcacttg gtttaaaaac 2340
aaccacaaaa tacaacaaga gcctggaatt attttaggac caggaagcag cacgctgttt 2400
attgaaagag tcacagaaga ggatgaaggt gtctatcact gcaaagccac caaccagaag 2460
ggctctgtgg aaagttcagc atacctcact gttcaaggaa cctcggacaa gtctaatctg 2520
gagctgatca ctctaacatg cacctgtgtg gctgcgactc tcttctggct cctattaacc 2580

ctccttatcc gaaaaatgaa aaggtcttct tctgaaataa agactgacta cctatcaatt 2640
ataatggacc cagatgaagt tcctttggat gagcagtgtg agcggctccc ttatgatgcc 2700
agcaagtggg agtttgcccg ggagagactt aaactgggca aatcacttgg aagaggggct 2760
tttggaaaag tggttcaagc atcagcattt ggcattaaga aatcacctac gtgccggact 2820
gtggctgtga aaatgctgaa agagggggcc acggccagcg agtacaaagc tctgatgact 2880
gagctaaaaa tcttgaccca cattggccac catctgaacg tggttaacct gctgggagcc 2940
tgcaccaagc aaggagggcc tctgatggtg attgttgaat actgcaaata tggaaatctc 3000
tccaactacc tcaagagcaa acgtgactta ttttttctca acaaggatgc agcactacac 3060
atggagccta agaaagaaaa aatggagcca ggcctggaac aaggcaagaa accaagacta 3120
gatagcgtca ccagcagcga aagctttgcg agctccggct ttcaggaaga taaaagtctg 3180
agtgatgttg aggaagagga ggattctgac ggtttctaca aggagcccat cactatggaa 3240
gatctgattt cttacagttt tcaagtggcc agaggcatgg agttcctgtc ttccagaaag 3300
tgcattcatc gggacctggc agcgagaaac attcttttat ctgagaacaa cgtggtgaag 3360
atttgtgatt ttggccttgc ccgggatatt tataagaacc ccgattatgt gagaaaagga 3420
gatactcgac ttcctctgaa atggatggct cccgaatcta tctttgacaa aatctacagc 3480
accaagagcg acgtgtggtc ttacggagta ttgctgtggg aaatcttctc cttaggtggg 3540
tctccatacc caggagtaca aatggatgag gacttttgca gtcgcctgag ggaaggcatg 3600
aggatgagag ctcctgagta ctctactcct gaaatctatc agatcatgct ggactgctgg 3660
cacagagacc caaaagaaag gccaagattt gcagaacttg tggaaaaact aggtgatttg 3720
cttcaagcaa atgtacaaca ggatggtaaa gactacatcc caatcaatgc catactgaca 3780
ggaaatagtg ggtttacata ctcaactcct gccttctctg aggacttctt caaggaaagt 3840
atttcagctc cgaagtttaa ttcaggaagc tctgatgatg tcagatatgt aaatgctttc 3900
aagttcatga gcctggaaag aatcaaaacc tttgaagaac ttttaccgaa tgccacctcc 3960
atgtttgatg actaccaggg cgacagcagc actctgttgg cctctcccat gctgaagcgc 4020
ttcacctgga ctgacagcaa acccaaggcc tcgctcaaga ttgacttgag agtaaccagt 4080
aaaagtaagg agtcggggct gtctgatgtc agcaggccca gtttctgcca ttccagctgt 4140
gggcacgtca gcgaaggcaa gcgcaggttc acctacgacc acgctgagct ggaaaggaaa 4200
atcgcgtgct gctccccgcc cccagactac aactcggtgg tcctgtactc caccccaccc 4260
atctagagtt tgacacgaag ccttatttct agaagcacat gtgtatttat acccccagga 4320
aactagcttt tgccagtatt atgcatatat aagtttacac ctttatcttt ccatgggagc 4380
cagctgcttt ttgtgatttt tttaatagtg cttttttttt ttgactaaca agaatgtaac 4440
tccagataga gaaatagtga caagtgaaga acactactgc taaatcctca tgttactcag 4500
tgttagagaa atccttccta aacccaatga cttccctgct ccaacccccg ccacctcagg 4560
gcacgcagga ccagtttgat tgaggagctg cactgatcac ccaatgcatc acgtacccca 4620
ctgggccagc cctgcagccc aaaacccagg gcaacaagcc cgttagcccc aggggatcac 4680
tggctggcct gagcaacatc tcgggagtcc tctagcaggc ctaagacatg tgaggaggaa 4740
aaggaaaaaa agcaaaaagc aagggagaaa agagaaaccg ggagaaggca tgagaaagaa 4800
tttgagacgc accatgtggg cacggagggg gacggggctc agcaatgcca tttcagtggc 4860
ttcccagctc tgacccttct acatttgagg gcccagccag gagcagatgg acagcgatga 4920
ggggacattt tctggattct gggaggcaag aaaaggacaa atatcttttt tggaactaaa 4980
gcaaatttta gacctttacc tatggaagtg gttctatgtc cattctcatt cgtggcatgt 5040
tttgatttgt agcactgagg gtggcactca actctgagcc catacttttg gctcctctag 5100
taagatgcac tgaaaactta gccagagtta ggttgtctcc aggccatgat ggccttacac 5160
tgaaaatgtc acattctatt ttgggtatta atatatagtc cagacactta actcaatttc 5220
ttggtattat tctgttttgc acagttagtt gtgaaagaaa gctgagaaga atgaaaatgc 5280
agtcctgagg agagttttct ccatatcaaa acgagggctg atggaggaaa aaggtcaata 5340
aggtcaaggg aagaccccgt ctctatacca accaaaccaa ttcaccaaca cagttgggac 5400
ccaaaacaca ggaagtcagt cacgtttcct tttcatttaa tggggattcc actatctcac 5460
actaatctga aaggatgtgg aagagcatta gctggcgcat attaagcact ttaagctcct 5520
tgagtaaaaa ggtggtatgt aatttatgca aggtatttct ccagttggga ctcaggatat 5580
tagttaatga gccatcacta gaagaaaagc ccattttcaa ctgctttgaa acttgcctgg 5640
ggtctgagca tgatgggaat agggagacag ggtaggaaag ggcgcctact cttcagggtc 5700
taaagatcaa gtgggccttg gatcgctaag ctggctctgt ttgatgctat ttatgcaagt 5760
tagggtctat gtattta 5777

<210> 158
<211> 4450
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM002020
<309> 2004-12-18

<400> 158
acccacgcgc agcggccgga gatgcagcgg ggcgccgcgc tgtgcctgcg actgtggctc 60
tgcctgggac tcctggacgg cctggtgagt gactactcca tgaccccccc gaccttgaac 120
atcacggagg agtcacacgt catcgacacc ggtgacagcc tgtccatctc ctgcagggga 180
cagcaccccc tcgagtgggc ttggccagga gctcaggagg cgccagccac cggagacaag 240
gacagcgagg acacgggggt ggtgcgagac tgcgagggca cagacgccag gccctactgc 300
aaggtgttgc tgctgcacga ggtacatgcc aacgacacag gcagctacgt ctgctactac 360
aagtacatca aggcacgcat cgagggcacc acggccgcca gctcctacgt gttcgtgaga 420
gactttgagc agccattcat caacaagcct gacacgctct tggtcaacag gaaggacgcc 480
atgtgggtgc cctgtctggt gtccatcccc ggcctcaatg tcacgctgcg ctcgcaaagc 540
tcggtgctgt ggccagacgg gcaggaggtg gtgtgggatg accggcgggg catgctctgtg 600
tccacgccac tgctgcacga tgccctgtac ctgcagtgcg agaccacctg gggagaccag 660
gacttccttt ccaacccctt cctggtgcac atcacaggca acgagctcta tgacatccag 720
ctgttgccca ggaagtcgct ggagctgctg gtaggggaga agctggtcct caactgcacc 780
gtgtgggctg agtttaactc aggtgtcacc tttgactggg actacccagg gaagcaggca 840
gagcggggta agtgggtgcc cgagcgacgc tcccaacaga cccacacaga actctccagc 900
atcctgacca tccacaacgt cagccagcac gacctgggct cgtatgtgtg caaggccaac 960
aacggcatcc agcgatttcg ggagagcacc gaggtcattg tgcatgaaaa tcccttcatc 1020
agcgtcgagt ggctcaaagg acccatcctg gaggccacgg caggagacga gctggtgaag 1080
ctgcccgtga agctggcagc gtaccccccg cccgagttcc agtggtacaa ggatggaaag 1140
gcactgtccg ggcgccacag tccacatgcc ctggtgctca aggaggtgac agaggccagc 1200
acaggcacct acaccctcgc cctgtggaac tccgctgctg gcctgaggcg caacatcagc 1260
ctggagctgg tggtgaatgt gccccccccag atacatgaga aggaggcctc ctcccccagc 1320
atctactcgc gtcacagccg ccaggccctc acctgcacgg cctacggggt gcccctgcct 1380
ctcagcatcc agtggcactg gcggccctgg acaccctgca agatgtttgc ccagcgtagt 1440
ctccggcggc ggcagcagca agacctcatg ccacagtgcc gtgactggag ggcggtgacc 1500
acgcaggatg ccgtgaaccc catcgagagc ctggacacct ggaccgagtt tgtggaggga 1560
aagaataaga ctgtgagcaa gctggtgatc cagaatgcca acgtgtctgc catgtacaag 1620
tgtgtggtct ccaacaaggt gggccaggat gagcggctca tctacttcta tgtgaccacc 1680
atccccgacg gcttcaccat cgaatccaag ccatccgagg agctactaga gggccagccg 1740
gtgctcctga gctgccaagc cgacagctac aagtacgagc atctgcgctg gtaccgcctc 1800
aacctgtcca cgctgcacga tgcgcacggg aacccgcttc tgctcgactg caagaacgtg 1860
catctgttcg ccacccctct ggccgccagc ctggaggagg tggcacctgg ggcgcgccac 1920
gccacgctca gcctgagtat cccccgcgtc gcgcccgagc acgagggcca ctatgtgtgc 1980
gaagtgcaag accggcgcag ccatgacaag cactgccaca agaagtacct gtcggtgcag 2040
gccctggaag cccctcggct cacgcagaac ttgaccgacc tcctggtgaa cgtgagcgac 2100
tcgctggaga tgcagtgctt ggtggccgga gcgcacgcgc ccagcatcgt gtggtacaaa 2160
gacgagaggc tgctggagga aaagtctgga gtcgacttgg cggactccaa ccagaagctg 2220
agcatccagc gcgtgcgcga ggaggatgcg ggaccgtatc tgtgcagcgt gtgcagaccc 2280
aagggctgcg tcaactcctc cgccagcgtg gccgtggaag gctccgagga taagggcagc 2340
atggagatcg tgatccttgt cggtaccggc gtcatcgctg tcttcttctg ggtcctcctc 2400
ctcctcatct tctgtaacat gaggaggccg gcccacgcag acatcaagac gggctacctg 2460
tccatcatca tggaccccgg ggaggtgcct ctggaggagc aatgcgaata cctgtcctac 2520
gatgccagcc agtgggaatt cccccgagag cggctgcacc tggggagagt gctcggctac 2580
ggcgccttcg ggaaggtggt ggaagcctcc gctttcggca tccacaaggg cagcagctgt 2640
gacaccgtgg ccgtgaaaat gctgaaagag ggcgccacgg ccagcgagca gcgcgcgctg 2700

atgtcggagc tcaagatcct cattcacatc ggcaaccacc tcaacgtggt caacctcctc 2760
ggggcgtgca ccaagccgca gggccccctc atggtgatcg tggagttctg caagtacggc 2820
aacctctcca acttcctgcg cgccaagcgg gacgccttca gcccctgcgc ggagaagtct 2880
cccgagcagc gcggacgctt ccgcgccatg gtggagctcg ccaggctgga tcggaggcgg 2940
ccggggagca gcgacagggt cctcttcgcg cggttctcga agaccgaggg cggagcgagg 3000
cgggcttctc cagaccaaga agctgaggac ctgtggctga gcccgctgac catggaagat 3060
cttgtctgct acagcttcca ggtggccaga gggatggagt tcctggcttc ccgaaagtgc 3120
atccacagag acctggctgc tcggaacatt ctgctgtcgg aaagcgacgt ggtgaagatc 3180
tgtgactttg gccttgcccg ggacatctac aaagaccccg actacgtccg caagggcagt 3240
gcccggctgc ccctgaagtg gatggccctt gaaagcatct tcgacaaggt gtacaccacg 3300
cagagtgacg tgtggtcctt tggggtgctt ctctgggaga tcttctctct gggggcctcc 3360
ccgtaccctg gggtgcagat caatgaggag ttctgccagc gcgtgagaga cggcacaagg 3420
atgagggccc cggagctggc cactcccgcc atacgccaca tcatgctgaa ctgctggtcc 3480
ggagacccca aggcgagacc tgcattctcg gacctggtgg agatcctggg ggacctgctc 3540
cagggcaggg gcctgcaaga ggaagaggag gtctgcatgg ccccgcgcag ctctcagagc 3600
tcagaagagg gcagcttctc gcaggtgtcc accatggccc tacacatcgc ccaggctgac 3660
gctgaggaca gcccgccaag cctgcagcgc cacagcctgg ccgccaggta ttacaactgg 3720
gtgtcctttc ccgggtgcct ggccagaggg gctgagaccc gtggttcctc caggatgaag 3780
acatttgagg aattccccat gaccccaacg acctacaaag gctctgtgga caaccagaca 3840
gacagtggga tggtgctggc ctcggaggag tttgagcaga tagagagcag gcatagacaa 3900
gaaagcggct tcaggtagct gaagcagaga gagagaaggc agcatacgtc agcattttct 3960
tctctgcact tataagaaag atcaaagact ttaagacttt cgctatttct tctactgcta 4020
tctactacaa acttcaaaga ggaaccagga ggacaagagg agcatgaaag tggacaagga 4080
gtgtgaccac tgaagcacca cagggagggg ttaggcctcc ggatgactgc gggcaggcct 4140
ggataatatc cagcctccca caagaagctg gtggagcaga gtgttccctg actcctccaa 4200
ggaaagggag acgccctttc atggtctgct gagtaacagg tgccttccca gacactggcg 4260
ttactgcttg accaaagagc cctcaagcgg cccttatgcc agcgtgacag agggctcacc 4320
tcttgccttc taggtcactt ctcacaatgt cccttcagca cctgaccctg tgcccgccga 4380
ttattccttg gtaatatgag taatacatca aagagtagta ttaaaagcta attaatcatg 4440
tttataaaaa 4450

<210> 159
<211> 4541
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM002447
<309> 2004-10-28

<400> 159
ggatcctcta gggtcccagc tcgcctcgat ggagctcctc ccgccgctgc ctcagtcctt 60
cctgttgctg ctgctgttgc ctgccaagcc cgcggcgggc gaggactggc agtgcccgcg 120
cacccctac gcggcctctc gcgactttga cgtgaagtac gtggtgccca gcttctccgc 180
cggaggcctg gtacaggcca tggtgaccta cgagggcgac agaaatgaga gtgctgtgtt 240
tgtagccata cgcaatcgcc tgcatgtgct tgggcctgac ctgaagtctg tccagagcct 300
ggccacgggc cctgctggag accctggctg ccagacgtgt gcagcctgtg gcccaggacc 360
ccacggccct cccggtgaca cagacacaaa ggtgctggtg ctggatcccg cgctgcctgc 420
gctggtcagt tgtggctcca gcctgcaggg ccgctgcttc ctgcatgacc tagagcccca 480
agggacagcc gtgcatctgg cagcgccagc ctgcctcttc tcagcccacc ataaccggcc 540
cgatgactgc cccgactgtg tggccagccc attgggcacc cgtgtaactg tggttgagca 600
aggccaggcc tcctatttct acgtggcatc ctcactggac gcagccgtgg ctggcagctt 660
cagcccacgc tcagtgtcta tcaggcgtct caaggctgac gcctcgggat tcgcaccggg 720
ctttgtggcg ttgtcagtgc tgcccaagca tcttgtctcc tacagtattg aatacgtgca 780
cagcttccac acgggagcct tcgtatactt cctgactgta cagccggcca gcgtgacaga 840
tgatcctagt gccctgcaca cacgcctggc acggcttagc gccactgagc cagagttggg 900

tgactatcgg gagctggtcc tcgactgcag atttgctcca aaacgcaggc gccgggggggc 960
cccagaaggc ggacagccct accctgtgct gcaggtggcc cactccgctc cagtgggtgc 1020
ccaacttgcc actgagctga gcatcgccga gggccaggaa gtactatttg gggtctttgt 1080
gactggcaag gatggtggtc ctggcgtggg ccccaactct gtcgtctgtg ccttccccat 1140
tgacctgctg gacacactaa ttgatgaggg tgtggagcgc tgttgtgaat ccccagtcca 1200
tccaggcctc cggcgaggcc tcgacttctt ccagtcgccc agtttttgcc ccaacccgcc 1260
tggcctggaa gccctcagcc ccaacaccag ctgccgccac ttccctctgc tggtcagtag 1320
cagcttctca cgtgtggacc tattcaatgg gctgttggga ccagtacagg tcactgcatt 1380
gtatgtgaca cgccttgaca acgtcacagt ggcacacatg ggcacaatgg atgggcgtat 1440
cctgcaggtg gagctggtca ggtcactaaa ctacttgctg tatgtgtcca acttctcact 1500
gggtgacagt gggcagcccg tgcagcggga tgtcagtcgt cttggggacc acctactctt 1560
tgcctctggg gaccaggttt tccaggtacc tatccgaggc cctggctgcc gccacttcct 1620
gacctgtggg cgttgcctaa gggcatggca tttcatgggc tgtggctggt gtgggaacat 1680
gtgcggccag cagaaggagt gtcctggctc ctggcaacag gaccactgcc cacctaagct 1740
tactgagttc caccccaca gtggacctct aaggggcagt acaaggctga ccctgtgtgg 1800
ctccaacttc taccttcacc cttctggtct ggtgcctgag ggaacccatc aggtcactgt 1860
gggccaaagt ccctgccggc cactgcccaa ggacagctca aaactcagac cagtgccccg 1920
gaaagacttt gtagaggagt ttgagtgtga actggagccc ttgggcaccc aggcagtggg 1980
gcctaccaac gtcagcctca ccgtgactaa catgccaccg ggcaagcact tccgggtaga 2040
cggcacctcc gtgctgagag gcttctcttt catggagcca gtgctgatag cagtgcaacc 2100
cctctttggc ccacgggcag gaggcacctg tctcactctt gaaggccaga gtctgtctgt 2160
aggcaccagc cgggctgtgc tggtcaatgg gactgagtgt ctgctagcac gggtcagtga 2220
ggggcagctt ttatgtgcca cacccctgg ggccacggtg gccagtgtcc cccttagcct 2280
gcaggtgggg ggtgcccagg tacctggttc ctggaccttc cagtacagag aagaccctgt 2340
cgtgctaagc atcagcccca actgtggcta catcaactcc cacatcacca tctgtggcca 2400
gcatctaact tcagcatggc acttagtgct gtcattccat gacgggctta gggcagtgga 2460
aagcaggtgt gagaggcagc ttccagagca gcagctgtgc cgccttcctg aatatgtggt 2520
ccgagacccc cagggatggg tggcagggaa tctgagtgcc cgaggggatg gagctgctgg 2580
ctttacactg cctggctttc gcttcctacc cccaccccat ccacccagtg ccaacctagt 2640
tccactgaag cctgaggagc atgccattaa gtttgagtat attgggctgg gcgctgtggc 2700
tgactgtgtg ggtatcaacg tgaccgtggg tggtgagagc tgccagcacg agttccgggg 2760
ggacatggtt gtctgccccc tgcccccatc cctgcagctt ggccaggatg gtgccccatt 2820
gcaggtctgc gtagatggtg aatgtcatat cctgggtaga gtggtgcggc cagggccaga 2880
tggggtccca cagagcacgc tccttggtat cctgctgcct ttgctgctgc ttgtggctgc 2940
actggcgact gcactggtct tcagctactg gtggcggagg aagcagctag ttcttcctcc 3000
caacctgaat gacctggcat ccctggacca gactgctgga gccacacccc tgcctattct 3060
gtactcgggc tctgactaca gaagtggcct tgcactccct gccattgatg gtctggattc 3120
caccacttgt gtccatggag catccttctc cgatagtgaa gatgaatcct gtgtgccact 3180
gctgcggaaa gagtccatcc agctaaggga cctggactct gcgctcttgg ctgaggtcaa 3240
ggatgtgctg attccccatg agcgggtggt cacccacagt gaccgagtca ttggcaaagg 3300
ccactttgga gttgtctacc acggagaata catagaccag gcccagaatc gaatccaatg 3360
tgccatcaag tcactaagtc gcatcacaga gatgcagcag gtggaggcct tcctgcgaga 3420
ggggctgctc atgcgtggcc tgaaccaccc gaatgtgctg gctctcattg gtatcatgtt 3480
gccacctgag ggcctgcccc atgtgctgct gccctatatg tgccacggtg acctgctcca 3540
gttcatccgc tcacctcagc ggaaccccac cgtgaaggac ctcatcagct ttggcctgca 3600
ggtagcccgc ggcatggagt acctggcaga gcagaagttt gtgcacaggg acctggctgc 3660
gcggaactgc atgctggacg agtcattcac agtcaaggtg gctgactttg gtttggcccg 3720
cgacatcctg gacagggagt actatagtgt tcaacagcat cgccacgctc gcctacctgt 3780
gaagtggatg gcgctggaga gcctgcagac ctatagattt accaccaagt ctgatgtgtg 3840
gtcatttggt gtgctgctgt gggaactgct gacacggggt gccccaccat accgccacat 3900
tgacccttt gaccttaccc acttcctggc ccagggtcgg cgcctgcccc agcctgagta 3960
ttgccctgat tctctgtacc aagtgatgca gcaatgctgg gaggcagacc cagcagtgcg 4020
acccaccttc agagtactag tgggggaggt ggagcagata gtgtctgcac tgcttgggga 4080
ccattatgtg cagctgccag caacctacat gaacttgggc cccagcacct cgcatgagat 4140
gaatgtgcgt ccagaacagc cgcagttctc acccatgcca gggaatgtac gccggccccg 4200
gccactctca gagcctcctc ggcccacttg acttagttct tgggctggac ctgcttagct 4260

gccttgagct aaccccaagg ctgcctctgg gccatgccag gccagagcag tggccctcca 4320
ccttgttcct gccctttaac tttcagaggc aataggtaaa tgggcccatt aggtccctca 4380
ctccacagag tgagccagtg agggcagtcc tgcaacatgt atttatggag tgcctgctgt 4440
ggaccctgtc ttctgggcac agtggactca gcagtgacca caccaacact gacccttgaa 4500
ccaataaagg aacaaatgac tattaaagca caaaaaaaaa a 4541

<210> 160
<211> 4138
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM000459
<309> 2004-10-26

<400> 160
cttctgtgct gttccttctt gcctctaact tgtaaacaag acgtactagg acgatgctaa 60
tggaaagtca caaaccgctg ggtttttgaa aggatccttg ggacctcatg cacatttgtg 120
gaaactggat ggagagattt ggggaagcat ggactcttta gccagcttag ttctctgtgg 180
agtcagcttg ctccttttctg gaactgtgga aggtgccatg gacttgatct tgatcaattc 240
cctacctctt gtatctgatg ctgaaacatc tctcacctgc attgcctctg ggtggcgccc 300
ccatgagccc atcaccatag gaagggactt tgaagcctta atgaaccagc accaggatcc 360
gctggaagtt actcaagatg tgaccagaga atgggctaaa aaagttgttt ggaagagaga 420
aaaggctagt aagatcaatg gtgcttattt ctgtgaaggg cgagttcgag gagaggcaat 480
caggatacga accatgaaga tgcgtcaaca agcttccttc ctaccagcta ctttaactat 540
gactgtggac aagggagata acgtgaacat atctttcaaa aaggtattga ttaaagaaga 600
agatgcagtg atttacaaaa atggttcctt catccattca gtgccccggc atgaagtacc 660
tgatattcta gaagtacacc tgcctcatgc tcagccccag gatgctggag tgtactcggc 720
caggtatata ggaggaaacc tcttcacctc ggccttcacc aggctgatag tccggagatg 780
tgaagcccag aagtggggac ctgaatgcaa ccatctctgt actgcttgta tgaacaatgg 840
tgtctgccat gaagatactg gagaatgcat ttgccctcct gggtttatgg gaaggacgtg 900
tgagaaggct tgtgaactgc acacgtttgg cagaacttgt aaagaaaggt gcagtggaca 960
agagggatgc aagtcttatg tgttctgtct ccctgacccc tatgggtgtt cctgtgccac 1020
aggctggaag ggtctgcagt gcaatgaagc atgccaccct ggtttttacg ggccagattg 1080
taagcttagg tgcagctgca acaatgggga gatgtgtgat cgcttccaag gatgtctctg 1140
ctctccagga tggcaggggc tccagtgtga gagagaaggc ataccgagga tgaccccaaa 1200
gatagtggat ttgccagatc atatagaagt aaacagtggt aaatttaatc ccatttgcaa 1260
agcttctggc tggccgctac ctactaatga agaaatgacc ctggtgaagc cggatgggac 1320
agtgctccat ccaaaagact ttaaccatac ggatcatttc tcagtagcca tattcaccat 1380
ccaccggatc ctccccccctg actcaggagt ttgggtctgc agtgtgaaca cagtggctgg 1440
gatggtggaa aagcccttca acatttctgt taaagttctt ccaaagcccc tgaatgcccc 1500
aaacgtgatt gacactggac ataactttgc tgtcatcaac atcagctctg agccttactt 1560
tggggatgga ccaatcaaat ccaagaagct tctatacaaa cccgttaatc actatgaggc 1620
ttggcaacat attcaagtga caaatgagat tgttacactc aactatttgg aacctcggac 1680
agaatatgaa ctctgtgtgc aactggtccg tcgtggagag ggtggggaag ggcatcctgg 1740
acctgtgaga cgcttcacaa cagcttctat cggactccct cctccaagag gtctaaatct 1800
cctgcctaaa agtcagacca ctctaaattt gacctggcaa ccaatatttc caagctcgga 1860
agatgacttt tatgttgaag tggagagaag gtctgtgcaa aaaagtgatc agcagaatat 1920
taaagttcca ggcaacttga cttcggtgct acttaacaac ttacatccca gggagcagta 1980
cgtggtccga gctagagtca acaccaaggc ccaggggggaa tggagtgaag atctcactgc 2040
ttggaccctt agtgacattc ttcctcctca accagaaaac atcaagattt ccaacattac 2100
acactcctcg gctgtgattt cttggacaat attggatggc tattctattt cttctattac 2160
tatccgttac aaggttcaag gcaagaatga agaccagcac gttgatgtga agataaagaa 2220
tgccaccatc attcagtatc agctcaaggg cctagagcct gaaacagcat accaggtgga 2280
cattttgca gagaacaaca tagggtcaag caacccagcc ttttctcatg aactggtgac 2340
cctcccagaa tctcaagcac cagcggacct cggaggggggg aagatgctgc ttatagccat 2400

ccttggctct gctggaatga cctgcctgac tgtgctgttg gcctttctga tcatattgca 2460
attgaagagg gcaaatgtgc aaaggagaat ggcccaagcc ttccaaaacg tgagggaaga 2520
accagctgtg cagttcaact cagggactct ggccctaaac aggaaggtca aaaacaaccc 2580
agatcctaca atttatccag tgcttgactg gaatgacatc aaatttcaag atgtgattgg 2640
ggagggcaat tttggccaag ttcttaaggc gcgcatcaag aaggatgggt tacggatgga 2700
tgctgccatc aaaagaatga aagaatatgc ctccaaagat gatcacaggg actttgcagg 2760
agaactggaa gttctttgta aacttggaca ccatccaaac atcatcaatc tcttaggagc 2820
atgtgaacat cgaggctact tgtacctggc cattgagtac gcgccccatg gaaaccttct 2880
ggacttcctt cgcaagagcc gtgtgctgga gacggaccca gcatttgcca ttgccaatag 2940
caccgcgtcc acactgtcct cccagcagct ccttcacttc gctgccgacg tggcccgggg 3000
catggactac ttgagccaaa aacagtttat ccacagggat ctggctgcca gaaacatttt 3060
agttggtgaa aactatgtgg caaaaatagc agattttgga ttgtcccgag gtcaagaggt 3120
gtacgtgaaa aagacaatgg gaaggctccc agtgcgctgg atggccatcg agtcactgaa 3180
ttacagtgtg tacacaacca acagtgatgt atggtcctat ggtgtgttac tatgggagat 3240
tgttagctta ggaggcacac cctactgcgg gatgacttgt gcagaactct acgagaagct 3300
gccccagggc tacagactgg agaagcccct gaactgtgat gatgaggtgt atgatctaat 3360
gagacaatgc tggcgggaga agccttatga gaggccatca tttgcccaga tattggtgtc 3420
cttaaacaga atgttagagg agcgaaagac ctacgtgaat accacgcttt atgagaagtt 3480
tacttatgca ggaattgact gttctgctga agaagcggcc taggacagaa catctgtata 3540
ccctctgttt ccctttcact ggcatgggag acccttgaca actgctgaga aaacatgcct 3600
ctgccaaagg atgtgatata taagtgtaca tatgtgctgg aattctaaca agtcataggt 3660
taatatttaa gacactgaaa aatctaagtg atataaatca gattcttctc tctcatttta 3720
tccctcacct gtagcatgcc agtcccgttt catttagtca tgtgaccact ctgtcttgtg 3780
tttccacagc ctgcaagttc agtccaggat gctaacatct aaaaatagac ttaaatctca 3840
ttgcttacaa gcctaagaat ctttagagaa gtatacataa gtttaggata aaataatggg 3900
attttctttt cttttctctg gtaatattga cttgtatatt ttaagaaata acagaaagcc 3960
tgggtgacat ttgggagaca tgtgacattt atatattgaa ttaatatccc tacatgtatt 4020
gcacattgta aaaagtttta gttttgatga gttgtgagtt taccttgtat actgtaggca 4080
cactttgcac tgatatatca tgagtgaata aatgtcttgc ctactcaaaa aaaaaaaa 4138

<210> 161
<211> 3960
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM005424
<309> 2004-12-18

<400> 161
cacaggctga gcagtcaggc ccacagcatc tgaccccagg cccagctcgt cctggctggc 60
ctgggtcggc ctctggagta tggtctggcg ggtgcccccc ttcttgctcc ccatcctctt 120
cttggcttct catgtgggcg cggcggtgga cctgacgctg ctggccaacc tgcggctcac 180
ggacccccag cgcttcttcc tgacttgcgt gtctggggag gccggggcgg ggaggggctc 240
ggacgcctgg ggcccgcccc tgctgctgga gaaggacgac cgtatcgtgc gcaccccgcc 300
cgggccaccc ctgcgcctgg cgcgcaacgg ttcgcaccag gtcacgcttc gcggcttctc 360
caagccctcg gacctcgtgg gcgtcttctc ctgcgtgggc ggtgctgggg cgcggcgcac 420
gcgcgtcatc tacgtgcaca acagccctgg agcccacctg cttccagaca aggtcacaca 480
cactgtgaac aaaggtgaca ccgctgtact ttctgcacgt gtgcacaagg agaagcagac 540
agacgtgatc tggaagagca acggatccta cttctacacc ctggactggc atgaagccca 600
ggatgggcgg ttcctgctgc agctcccaaa tgtgcagcca ccatcgagcg gcatctacag 660
tgccacttac ctggaagcca gccccctggg cagcgccttc tttcggctca tcgtgcgggg 720
ttgtggggct gggcgctggg ggccaggctg taccaaggag tgcccaggtt gcctacatgg 780
aggtgtctgc cacgaccatg acggcgaatg tgtatgcccc cctggcttca ctggcacccg 840
ctgtgaacag gcctgcagag agggccgttt tgggcagagc tgccaggagc agtgcccagg 900
catatcaggc tgccggggcc tcaccttctg cctcccagac ccctatggct gctcttgtgg 960

atctggctgg agaggaagcc agtgccaaga agcttgtgcc cctggtcatt ttggggctga 1020
ttgccgactc cagtgccagt gtcagaatgg tggcacttgt gaccggttca gtggttgtgt 1080
ctgcccctct gggtggcatg gagtgcactg tgagaagtca gaccggatcc cccagatcct 1140
caacatggcc tcagaactgg agttcaactt agagacgatg ccccggatca actgtgcagc 1200
tgcagggaac cccttccccg tgcggggcag catagagcta cgcaagccag acggcactgt 1260
gctcctgtcc accaaggcca ttgtggagcc agagaagacc acagctgagt tcgaggtgcc 1320
ccgcttggtt cttgcggaca gtgggttctg ggagtgccgt gtgtccacat ctggcggcca 1380
agacagccgg cgcttcaagg tcaatgtgaa agtgcccccc gtgcccctgg ctgcacctcg 1440
gctcctgacc aagcagagcc gccagcttgt ggtctccccg ctggtctcgt tctctgggga 1500
tggacccatc tccactgtcc gcctgcacta ccggccccag gacagtacca tggactggtc 1560
gaccattgtg gtggacccca gtgagaacgt gacgttaatg aacctgaggc caaagacagg 1620
atacagtgtt cgtgtgcagc tgagccggcc aggggaagga ggagaggggg cctgggggcc 1680
tcccaccctc atgaccacag actgtcctga gcctttgttg cagccgtggt tggagggctg 1740
gcatgtggaa ggcactgacc ggctgcgagt gagctggtcc ttgcccttgg tgcccgggcc 1800
actggtgggc gacggtttcc tgctgcgcct gtgggacggg acacgggggc aggagcggcg 1860
ggagaacgtc tcatcccccc aggcccgcac tgccctcctg acgggactca cgcctggcac 1920
ccactaccag ctggatgtgc agctctacca ctgcaccctc ctgggcccgg cctcgccccc 1980
tgcacacgtg cttctgcccc ccagtgggcc tccagccccc cgacacctcc acgcccaggc 2040
cctctcagac tccgagatcc agctgacatg gaagcacccg gaggctctgc ctgggccaat 2100
atccaagtac gttgtggagg tgcaggtggc tgggggtgca ggagacccac tgtggataga 2160
cgtggacagg cctgaggaga caagcaccat catccgtggc ctcaacgcca gcacgcgcta 2220
cctcttccgc atgcgggcca gcattcaggg gctcggggac tggagcaaca cagtagaaga 2280
gtccaccctg ggcaacgggc tgcaggctga gggcccagtc caagagagcc gggcagctga 2340
agagggcctg gatcagcagc tgatcctggc ggtggtgggc tccgtgtctg ccacctgcct 2400
caccatcctg gccgcccttt taaccctggt gtgcatccgc agaagctgcc tgcatcggag 2460
acgcaccttc acctaccagt caggctcggg cgaggagacc atcctgcagt tcagctcagg 2520
gaccttgaca cttacccggc ggccaaaact gcagcccgag cccctgagct acccagtgct 2580
agagtgggag gacatcacct ttgaggacct catcggggag gggaacttcg gccaggtcat 2640
ccgggccatg atcaagaagg acgggctgaa gatgaacgca gccatcaaaa tgctgaaaga 2700
gtatgcctct gaaaatgacc atcgtgactt tgcgggagaa ctggaagttc tgtgcaaatt 2760
ggggcatcac cccaacatca tcaacctcct gggggcctgt aagaaccgag gttacttgta 2820
tatcgctatt gaatatgccc cctacgggaa cctgctagat tttctgcgga aaagccgggt 2880
cctagagact gacccagctt ttgctcgaga gcatgggaca gcctctaccc ttagctcccg 2940
gcagctgctg cgtttcgcca gtgatgcggc caatggcatg cagtacctga gtgagaagca 3000
gttcatccac agggacctgg ctgcccggaa tgtgctggtc ggagagaacc tagcctccaa 3060
gattgcagac ttcggccttt ctcggggaga ggaggtttat gtgaagaaga cgatggggcg 3120
tctccctgtg cgctggatgg ccattgagtc cctgaactac agtgtctata ccaccaagag 3180
tgatgtctgg tcctttggag tccttctttg ggagatagtg agccttggag gtacacccta 3240
ctgtggcatg acctgtgccg agctctatga aaagctgccc cagggctacc gcatggagca 3300
gcctcgaaac tgtgacgatg aagtgtacga gctgatgcgt cagtgctggc gggaccgtcc 3360
ctatgagcga ccccccttg cccagattgc gctacagcta ggccgcatgc tggaagccag 3420
gaaggcctat gtgaacatgt cgctgtttga gaacttcact tacgcgggca ttgatgccac 3480
agctgaggag gcctgagctg ccatccagcc agaacgtggc tctgctggcc ggagcaaact 3540
ctgctgtcta acctgtgacc agtctgaccc ttacagcctc tgacttaagc tgcctcaagg 3600
aatttttta acttaaggga gaaaaaaagg gatctgggga tggggtgggc ttaggggaac 3660
tgggttccca tgctttgtag gtgtctcata gctatcctgg gcatccttct ttctagttca 3720
gctgccccac aggtgtgttt cccatcccac tgctccccca acacaaaccc ccactccagc 3780
tccttcgctt aagccagcac tcacaccact aacatgccct gttcagctac tcccactccc 3840
ggcctgtcat tcagaaaaaa ataaatgttc taataagctc caaaaaaaaa aaaaaaaaaa 3900
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3960

<210> 162
<211> 3985
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM005211
<309> 2004-10-26

<400> 162
gaagggcaga cagagtgtcc aaaagcgtga gagcacgaag tgaggagaag gtggagaaga 60
gagaagagga agaggaagag gaagagagga agcggaggga actgcggcca ggctaaaagg 120
ggaagaagag gatcagccca aggaggagga agaggaaaac aagacaaaca gccagtgcag 180
aggagaggaa cgtgtgtcca gtgtcccgat ccctgcggag ctagtagctg agagctctgt 240
gccctgggca ccttgcagcc ctgcacctgc ctgccacttc cccaccgagg ccatgggccc 300
aggagttctg ctgctcctgc tggtggccac agcttggcat ggtcagggaa tcccagtgat 360
agagcccagt gtccctgagc tggtcgtgaa gccaggagca acggtgacct tgcgatgtgt 420
gggcaatggc agcgtggaat gggatggccc cccatcacct cactggaccc tgtactctga 480
tggctccagc agcatcctca gcaccaacaa cgctaccttc caaaacacgg ggacctatcg 540
ctgcactgag cctggagacc ccctgggagg cagcgccgcc atccacctct atgtcaaaga 600
ccctgcccgg ccctggaacg tgctagcaca ggaggtggtc gtgttcgagg accaggacgc 660
actactgccc tgtctgctca cagacccggt gctggaagca ggcgtctcgc tggtgcgtgt 720
gcgtggccgg cccctcatgc gccacaccaa ctactccttc tcgccctggc atggcttcac 780
catccacagg gccaagttca ttcagagcca ggactatcaa tgcagtgccc tgatgggtgg 840
caggaaggtg atgtccatca gcatccggct gaaagtgcag aaagtcatcc cagggccccc 900
agccttgaca ctggtgcctg cagagctggt gcggattcga ggggaggctg cccagatcgt 960
gtgctcagcc agcagcgttg atgttaactt tgatgtcttc ctccaacaca acaacaccaa 1020
gctcgcaatc cctcaacaat ctgactttca taataaccgt taccaaaaag tcctgaccct 1080
caacctcgat caagtagatt tccaacatgc cggcaactac tcctgcgtgg ccagcaacgt 1140
gcagggcaag cactccacct ccatgttctt ccgggtggta gagagtgcct acttgaactt 1200
gagctctgag cagaacctca tccaggaggt gaccgtgggg gaggggctca acctcaaagt 1260
catggtggag gcctacccag gcctgcaagg ttttaactgg acctacctgg gacccttttc 1320
tgaccaccag cctgagccca agcttgctaa tgctaccacc aaggacacat acaggcacac 1380
cttcaccctc tctctgcccc gcctgaagcc ctctgaggct ggccgctact ccttcctggc 1440
cagaaaccca ggaggctgga gagctctgac gtttgagctc acccttcgat acccccaga 1500
ggtaagcgtc atatggacat tcatcaacgg ctctggcacc cttttgtgtg ctgcctctgg 1560
gtacccccag cccaacgtga catggctgca gtgcagtggc cacactgata ggtgtgatga 1620
ggcccaagtg ctgcaggtct gggatgaccc ataccctgag gtcctgagcc aggagccctt 1680
ccacaaggtg acggtgcaga gcctgctgac tgttgagacc ttagagcaca accaaaccta 1740
cgagtgcagg gcccacaaca gcgtggggag tggctcctgg gccttcatac ccatctctgc 1800
aggagcccac acgcatcccc cggatgagtt cctcttcaca ccagtggtgg tcgcctgcat 1860
gtccatcatg gccttgctgc tgctgctgct cctgctgcta ttgtacaagt ataagcagaa 1920
gcccaagtac caggtccgct ggaagatcat cgagagctat gagggcaaca gttatacttt 1980
catcgacccc acgcagctgc cttacaacga gaagtgggag ttcccccgga acaacctgca 2040
gtttggtaag accctcggag ctggagcctt tgggaaggtg gtggaggcca cggcctttgg 2100
tctgggcaag gaggatgctg tcctgaaggt ggctgtgaag atgctgaagt ccacggccca 2160
tgctgatgag aaggaggccc tcatgtccga gctgaagatc atgagccacc tgggccagca 2220
cgagaacatc gtcaaccttc tgggagcctg tacccatgga ggccctgtac tggtcatcac 2280
ggagtactgt tgctatggcg acctgctcaa ctttctgcga aggaaggctg aggccatgct 2340
gggacccagc ctgagccccg gccaggaccc cgagggaggc gtcgactata agaacatcca 2400
cctcgagaag aaatatgtcc gcagggacag tggcttctcc agccagggtg tggacaccta 2460
tgtggagatg aggcctgtct ccacttcttc aaatgactcc ttctctgagc aagacctgga 2520
caaggaggat ggacggcccc tggagctccg ggacctgctt cacttctcca gccaagtagc 2580
ccagggcatg gccttcctcg cttccaagaa ttgcatccac cgggacgtgg cagcgcgtaa 2640
cgtgctgttg accaatggtc atgtggccaa gattggggac ttcgggctgg ctagggacat 2700
catgaatgac tccaactaca ttgtcaaggg caatgcccgc ctgcctgtga agtggatggc 2760
cccagagagc atctttgact gtgtctacac ggttcagagc gacgtctggt cctatggcat 2820
cctcctctgg gagatcttct cacttgggct gaatccctac cctggcatcc tggtgaacag 2880
caagttctat aaactggtga aggatggata ccaaatggcc cagcctgcat ttgccccaaa 2940
gaatatatac agcatcatgc aggcctgctg ggccttggag cccacccaca gacccacctt 3000

ccagcagatc tgctccttcc ttcaggagca ggcccaagag gacaggagag agcgggacta 3060
taccaatctg ccgagcagca gcagaagcgg tggcagcggc agcagcagca gtgagctgga 3120
ggaggagagc tctagtgagc acctgacctg ctgcgagcaa ggggatatcg cccagccctt 3180
gctgcagccc aacaactatc agttctgctg aggagttgac gacagggagt accactctcc 3240
cctcctccaa acttcaactc ctccatggat ggggcgacac ggggagaaca tacaaactct 3300
gccttcggtc atttcactca acagctcggc ccagctctga aacttgggaa ggtgagggat 3360
tcaggggagg tcagaggatc ccacttcctg agcatgggcc atcactgcca gtcaggggct 3420
gggggctgag ccctcacccc cccctccct actgttctca tggtgttggc ctcgtgtttg 3480
ctatgccaac tagtagaacc ttctttccta atccccttat cttcatggaa atggactgac 3540
tttatgccta tgaagtcccc aggagctaca ctgatactga gaaaaccagg ctctttgggg 3600
ctagacagac tggcagagag tgagatctcc ctctctgaga ggagcagcag atgctcacag 3660
accacactca gctcaggccc cttggagcag gatggctcct ctaagaatct cacaggacct 3720
cttagtctct gccctatacg ccgccttcac tccacagcct caccctccc acccccatac 3780
tggtactgct gtaatgagcc aagtggcagc taaaagttgg gggtgttctg cccagtcccg 3840
tcattctggg ctagaaggca ggggaccttg gcatgtggct ggccacacca agcaggaagc 3900
acaaactccc ccaagctgac tcatcctaac taacagtcac gccgtgggat gtctctgtcc 3960
acattaaact aacagcatta atgca 3985

<210> 163
<211> 5598
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM002609
<309> 2004-10-26

<400> 163
ggcccctcag ccctgctgcc cagcacgagc ctgtgctcgc cctgcccaac gcagacagcc 60
agacccaggg cggccctct ggcggctctg ctcctcccga aggatgcttg gggagtgagg 120
cgaagctggg cgctcctctc ccctacagca gccccccttcc tccatccctc tgttctcctg 180
agccttcagg agcctgcacc agtcctgcct gtccttctac tcagctgtta cccactctgg 240
gaccagcagt ctttctgata actgggagag ggcagtaagg aggacttcct ggaggggtg 300
actgtccaga gcctggaact gtgcccacac cagaagccat cagcagcaag gacaccatgc 360
ggcttccggg tgcgatgcca gctctggccc tcaaaggcga gctgctgttg ctgtctctcc 420
tgttacttct ggaaccacag atctctcagg gcctggtcgt cacacccccg gggccagagc 480
ttgtcctcaa tgtctccagc accttcgttc tgacctgctc gggttcagct ccggtggtgt 540
gggaacggat gtcccaggag cccccacagg aaatggccaa ggcccaggat ggcaccttct 600
ccagcgtgct cacactgacc aacctcactg ggctagacac gggagaatac ttttgcaccc 660
acaatgactc ccgtggactg gagaccgatg agcggaaacg gctctacatc tttgtgccag 720
atcccaccgt gggcttcctc cctaatgatg ccgaggaact attcatcttt ctcacggaaa 780
taactgagat caccattcca tgccgagtaa cagacccaca gctggtggtg acactgcacg 840
agaagaaagg ggacgttgca ctgcctgtcc cctatgatca ccaacgtggc ttttctggta 900
tctttgagga cagaagctac atctgcaaaa ccaccattgg ggacagggag gtggattctg 960
atgcctacta tgtctacaga ctccaggtgt catccatcaa cgtctctgtg aacgcagtgc 1020
agactgtggt ccgccagggt gagaacatca ccctcatgtg cattgtgatc gggaatgagg 1080
tggtcaactt cgagtggaca tacccccgca aagaaagtgg gcggctggtg gagccggtga 1140
ctgacttcct cttggatatg ccttaccaca tccgctccat cctgcacatc cccagtgccg 1200
agttagaaga ctcggggacc tacacctgca atgtgacgga gagtgtgaat gaccatcagg 1260
atgaaaaggc catcaacatc accgtggttg agagcggcta cgtgcggctc ctgggagagg 1320
tgggcacact acaatttgct gagctgcatc ggagccggac actgcaggta gtgttcgagg 1380
cctacccacc gcccactgtc ctgtggttca aagacaaccg caccctgggc gactccagcg 1440
ctggcgaaat cgccctgtcc acgcgcaacg tgtcggagac ccggtatgtg tcagagctga 1500
cactggttcg cgtgaaggtg gcagaggctg gccactacac catgcgggcc ttccatgagg 1560
atgctgaggt ccagctctcc ttccagctac agatcaatgt ccctgtccga gtgctggagc 1620
taagtgagag ccaccctgac agtggggaac agacagtccg ctgtcgtggc cggggcatgc 1680

cccagccgaa catcatctgg tctgcctgca gagacctcaa aaggtgtcca cgtgagctgc 1740
cgcccacgct gctggggaac agttccgaag aggagagcca gctggagact aacgtgacgt 1800
actgggagga ggagcaggag tttgaggtgg tgagcacact gcgtctgcag cacgtggatc 1860
ggccactgtc ggtgcgctgc acgctgcgca acgctgtggg ccaggacacg caggaggtca 1920
tcgtggtgcc acactccttg ccctttaagg tggtggtgat ctcagccatc ctggccctgg 1980
tggtgctcac catcatctcc cttatcatcc tcatcatgct ttggcagaag aagccacgtt 2040
acgagatccg atggaaggtg attgagtctg tgagctctga cggccatgag tacatctacg 2100
tggaccccat gcagctgccc tatgactcca cgtgggagct gccgcgggac cagcttgtgc 2160
tgggacgcac cctcggctct ggggcctttg ggcaggtggt ggaggccacg gctcatggcc 2220
tgagccattc tcaggccacg atgaaagtgg ccgtcaagat gcttaaatcc acagcccgca 2280
gcagtgagaa gcaagccctt atgtcggagc tgaagatcat gagtcacctt gggccccacc 2340
tgaacgtggt caacctgttg ggggcctgca ccaaaggagg acccatctat atcatcactg 2400
agtactgccg ctacggagac ctggtggact acctgcaccg caacaaacac accttcctgc 2460
agcaccactc cgacaagcgc cgcccgccca gcgcggagct ctacagcaat gctctgcccg 2520
ttgggctccc cctgcccagc catgtgtcct tgaccgggga gagcgacggt ggctacatgg 2580
acatgagcaa ggacgagtcg gtggactatg tgcccatgct ggacatgaaa ggagacgtca 2640
aatatgcaga catcgagtcc tccaactaca tggcccctta cgataactac gttccctctg 2700
cccctgagag gacctgccga gcaactttga tcaacgagtc tccagtgcta agctacatgg 2760
acctcgtggg cttcagctac caggtggcca atggcatgga gtttctggcc tccaagaact 2820
gcgtccacag agacctggcg gctaggaacg tgctcatctg tgaaggcaag ctggtcaaga 2880
tctgtgactt tggcctggct cgagacatca tgcgggactc gaattacatc tccaaaggca 2940
gcaccttttt gcctttaaag tggatggctc cggagagcat cttcaacagc ctctacacca 3000
ccctgagcga cgtgtggtcc ttcgggatcc tgctctggga gatcttcacc ttgggtggca 3060
ccccttaccc agagctgccc atgaacgagc agttctacaa tgccatcaaa cggggttacc 3120
gcatggccca gcctgcccat gcctccgacg agatctatga gatcatgcag aagtgctggg 3180
aagagaagtt tgagattcgg ccccccttct cccagctggt gctgcttctc gagagactgt 3240
tgggcgaagg ttacaaaaag aagtaccagc aggtggatga ggagtttctg aggagtgacc 3300
acccagccat ccttcggtcc caggcccgct tgcctgggtt ccatggcctc cgatctcccc 3360
tggacaccag ctccgtcctc tatactgccg tgcagcccaa tgagggtgac aacgactata 3420
tcatcccccc gcctgacccc aaacccgagg ttgctgacga gggcccactg gagggttccc 3480
ccagcctagc cagctccacc ctgaatgaag tcaacacctc ctcaaccatc tcctgtgaca 3540
gccccctgga gccccaggac gaaccagagc cagagcccca gcttgagctc caggtggagc 3600
cggagccaga gctggaacag ttgccggatt cggggtgccc tgcgcctcgg gcggaagcag 3660
aggatagctt cctgtagggg gctggccccc accctgccct gcctgaagct ccccccctgc 3720
cagcacccag catctcctgg cctggcctga ccgggcttcc tgtcagccag gctgccctta 3780
tcagctgtcc ccttctggaa gctttctgct cctgacgtgt tgtgccccaa accctggggc 3840
tggcttagga ggcaagaaaa ctgcaggggc cgtgaccagc cctctgcctc cagggaggcc 3900
aactgactct gagccagggt tcccccaggg aactcagttt tcccatatgt aagatgggaa 3960
agttaggctt gatgacccag aatctaggat tctctccctg gctgacaggt ggggagaccg 4020
aatccctccc tgggaagatt cttggagtta ctgaggtggt aaattaactt ttttctgttc 4080
agccagctac ccctcaagga atcatagctc tctcctcgca ctttttatcc acccaggagc 4140
tagggaagag accctagcct ccctggctgc tggctgagct agggcctagc cttgagcagt 4200
gttgcctcat ccagaagaaa gccagtctcc tccctatgat gccagtccct gcgttccctg 4260
gcccgagctg gtctggggcc attaggcagc ctaattaatg ctggaggctg agccaagtac 4320
aggacacccc cagcctgcag cccttgccca gggcacttgg agcacacgca gccatagcaa 4380
gtgcctgtgt ccctgtcctt caggcccatc agtcctgggg ctttttcttt atcaccctca 4440
gtcttaatcc atccaccaga gtctagaagg ccagacgggc cccgcatctg tgatgagaat 4500
gtaaatgtgc cagtgtggag tggccacgtg tgtgtgccag tatatggccc tggctctgca 4560
ttggacctgc tatgaggctt tggaggaatc cctcaccctc tctgggcctc agtttcccct 4620
tcaaaaaatg aataagtcgg acttattaac tctgagtgcc ttgccagcac taacattcta 4680
gagtattcca ggtggttgca catttgtcca gatgaagcaa ggccatatac cctaaacttc 4740
catcctgggg gtcagctggg ctcctgggag attccagatc acacatcaca ctctggggac 4800
tcaggaacca tgccccttcc ccaggccccc agcaagtctc aagaacacag ctgcacaggc 4860
cttgacttag agtgacagcc ggtgtcctgg aaagccccaa gcagctgccc cagggacatg 4920
ggaagaccac gggacctctt tcactaccca cgatgacctc cgggggtatc ctgggcaaaa 4980
gggacaaaga gggcaaatga gatcacctcc tgcagcccac cactccagca cctgtgccga 5040

ggtctgcgtc gaagacagaa tggacagtga ggacagttat gtcttgtaaa agacaagaag 5100
cttcagatgg taccccaaga aggatgtgag aggtggccgc ttggagtttg cccctcaccc 5160
accagctgcc ccatccctga ggcagcgctc catgggggta tggttttgtc actgcccaga 5220
cctagcagtg acatctcatt gtccccagcc cagtgggcat tggaggtgcc aggggagtca 5280
gggttgtagc caagacgccc ccgcacgggg agggttggga agggggtgca ggaagctcaa 5340
cccctctggg caccaaccct gcattgcagg ttggcacctt acttccctgg gatccccaga 5400
gttggtccaa ggagggagag tgggttctca atacggtacc aaagatataa tcacctaggt 5460
ttacaaatat ttttaggact cacgttaact cacatttata cagcagaaat gctattttgt 5520
atgctgttaa gtttttctat ctgtgtactt ttttttaagg gaaagatttt aatattaaac 5580
ctggtgcttc tcactcac 5598

<210> 164
<211> 3343
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. M34641
<309> 2001-12-14

<400> 164
gaattcggga tgtggagctg gaagtgcctc ctcttctggg ctgtgctggt cacagccaca 60
ctctgcaccg ctaggccgtc cccgaccttg cctgaacaag cccagccctg gggagccccc 120
gtggaagtgg agtccttcct ggtccacccc ggtgacctgc tgcagcttcg ctgtcggctg 180
cgggacgatg tgcagagcat caactggctg cgggacgggg tgcagctggc ggaaagcaac 240
cgcacccgca tcacagggga ggaggtggag gtgcaggact ccgtgcccgc agactccggc 300
ctctatgctt gcgtaaccag cagcccctcg ggcagtgaca ccacctactt ctccgtcaat 360
gtttcagatg ctctcccctc ctcggaggat gatgatgatg atgatgactc ctcttcagag 420
gagaaagaaa cagataacac caaaccaaac cccgtagctc catattggac atccccagaa 480
aagatggaaa agaaattgca tgcagtgccg gctgccaaga cagtgaagtt caaatgccct 540
tccagtggga ccccaaaccc cacactgcgc tggttgaaaa atagcaaaga attcaaacct 600
gaccacagaa ttggaggcta caaggtccgt tatgccacct ggagcatcat aatggactct 660
gtggtgccct ctgacaaggg caactacacc tgcattgtgg agaatgagta cggcagcatc 720
aaccacacat accagctgga tgtcgtggag cggtcccctc accggcccat cctgcaagca 780
gggttgcccg ccaacaaaac agtggccctg ggtagcaacg tggagttcat gtgtaaggtg 840
tacagtgacc cgcagccgca catccagtgg ctaaagcaca tcgaggtgaa tgggagcaag 900
attggcccag acaacctgcc ttatgtccag atcttgaaga ctgctggagt taataccacc 960
gacaaagaga tggaggtgct tcacttaaga aatgtctcct ttgaggacgc aggggagtat 1020
acgtgcttgg cgggtaactc tatcggactc tcccatcact ctgcatggtt gaccgttctg 1080
gaagccctgg aagagaggcc ggcagtgatg acctcgcccc tgtacctgga gatcatcatc 1140
tattgcacag gggccttcct catctcctgc atggtggggt cggtcatcgt ctacaagatg 1200
aagagtggta ccaagaagag tgacttccac agccagatgg ctgtgcacaa gctggccaag 1260
agcatccctc tgcgcagaca ggtaacagtg tctgctgact ccagtgcatc catgaactct 1320
ggggttcttc tggttcggcc atcacggctc tcctccagtg ggactcccat gctagcaggg 1380
gtctctgagt atgagcttcc cgaagaccct cgctgggagc tgcctcggga cagactggtc 1440
ttaggcaaac ccctgggaga gggctgcttt gggcaggtgg tgttggcaga ggctatcggg 1500
ctggacaagg acaaacccaa ccgtgtgacc aaagtggctg tgaagatgtt gaagtcggac 1560
gcaacagaga aagacttgtc agacctgatc tcagaaatgg agatgatgaa gatgatcggg 1620
aagcataaga atatcatcaa cctgctgggg gcctgcacgc aggatggtcc cttgtatgtc 1680
atcgtggagt atgcctccaa gggcaacctg cgggagtacc tgcaggcccg gaggccccca 1740
gggctggaat actgctacaa ccccagccac aacccagagg agcagctctc ctccaaggac 1800
ctggtgtcct gcgcctacca ggtggcccga ggcatggagt atctggcctc caagaagtgc 1860
atacaccgag acctggcagc caggaatgtc ctggtgacag aggacaatgt gatgaagata 1920
gcagactttg gcctcgcacg ggacattcac cacatcgact actataaaaa gacaaccaac 1980

ggccgactgc ctgtgaagtg gatggcaccc gaggcattat ttgaccggat ctacacccac 2040
cagagtgatg tgtggtcttt cggggtgctc ctgtgggaga tcttcactct gggcggctcc 2100
ccataccccg gtgtgcctgt ggaggaactt ttcaagctgc tgaaggaggg tcaccgcatg 2160
gacaagccca gtaactgcac caacgagctg tacatgatga tgcgggactg ctggcatgca 2220
gtgccctcac agagacccac cttcaagcag ctggtggaag acctggaccg catcgtggcc 2280
ttgacctcca accaggagta cctggacctg tccatgcccc tggaccagta ctcccccagc 2340
tttcccgaca cccggagctc tacgtgctcc tcaggggagg attccgtctt ctctcatgag 2400
ccgctgcccg aggagccctg cctgccccga cacccagccc agcttgccaa tggcggactc 2460
aaacgccgct gactgccacc cacacgccct ccccagactc caccgtcagc tgtaaccctc 2520
acccacagcc cctgctgggc ccaccacctg tccgtccctg tcccctttcc tgctggcagg 2580
agccggctgc ctaccagggg ccttcctgtg tggcctgcct tcaccccact cagctcacct 2640
ctccctccac ctcctctcca cctgctggtg agaggtgcaa agaggcagat ctttgctgcc 2700
agccacttca tcccctccca gatgttggac caacacccct ccctgccaca gcatcgcctg 2760
gagggcaggg agtgggagcc aatgaacagg catgcaagtg agagcttcct gagctttctc 2820
tgtcggtttg gtctgttttg ccttcaccca taagcccctc gcactctggt ggcaggtgcc 2880
ttgtcctcag ggctacagca gtagggaggt cagtgcttcg tgcctcgatt gaaggtgacc 2940
tctgccccag ataggtggtg cagtggctta ttaattccga tactagtttg ctttgctgac 3000
caaatgcctg gtaccagagg atggtgaggc gaaggccagg ttgggggcag tgttgtggcc 3060
ctggggccag ccccaaactg ggggctctgt atatagctat gaagaaaaca caaagtgtat 3120
aaatctgagt atatatttac atgtcttttt aaaagggtcg ttaccagaga tttacccatc 3180
gggtaagatg ctcctggtgg ctgggaggca tcagttgcta tatattaaaa acaaaaaaga 3240
aaaaaaagga aaatgttttt aaaaaggtca tatatttttt gctacttttg ctgttttatt 3300
tttttaaatt atgttctaaa ctcgtgccgc tcgtgccgaa ttc 3343

<210> 165
<211> 3363
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM005232
<309> 2004-11-29

<400> 165
gcccccgccc ggcccgcccc gctctcctag tcccttgcaa cctggcgctg ccatccgggc 60
cactgtccca ggtcccggcc cggagctatg gagcggcgct ggcccctggg gctagggctg 120
gtgctgctgc tctgcgcccc gctgcccccg ggggcgcgcg ccaaggaagt tactctgatg 180
gacacaagca aggcacaggg agagctgggc tggctgctgg atcccccaaa agatgggtgg 240
agtgaacagc aacagatact gaatgggaca cccctgtaca tgtaccagga ctgcccaatg 300
caaggacgca gagacactga ccactggctt cgctccaatt ggatctaccg cggggaggag 360
gcttcccgcg tccacgtgga gctgcagttc accgtgcggg actgcaagag tttccctggg 420
ggagccgggc ctctgggctg caaggagacc ttcaaccttc tgtacatgga gagtgaccag 480
gatgtgggca ttcagctccg acggcccttg ttccagaagg taaccacggt ggctgcagac 540
cagagcttca ccattcgaga ccttgcgtct ggctccgtga agctgaatgt ggagcgctgc 600
tctctgggcc gcctgacccg ccgtggcctc tacctcgctt tccacaaccc gggtgcctgt 660
gtggccctgg tgtctgtccg ggtcttctac cagcgctgtc ctgagaccct gaatggcttg 720
gcccaattcc cagacactct gcctggcccc gctgggttgg tggaagtggc ggggacctgc 780
ttgccccacg cgcgggccag ccccaggccc tcaggtgcac cccgcatgca ctgcagccct 840
gatggcgagt ggctggtgcc tgtaggacgg tgccactgtg agcctggcta tgaggaaggt 900
ggcagtggcg aagcatgtgt tgcctgccct agcggctcct accggatgga catggacaca 960
ccccattgtc tcacgtgccc ccagcagagc actgctgagt ctgaggggggc caccatctgt 1020
acctgtgaga gcggccatta cagagctccc ggggagggcc cccaggtggc atgcacaggt 1080
ccccccctcgg ccccccgaaa cctgagcttc tctgcctcag ggactcagct ctccctgcgt 1140
tgggaacccc cagcagatac ggggggacgc caggatgtca gatacagtgt gaggtgttcc 1200
cagtgtcagg gcacagcaca ggacgggggg ccctgccagc cctgtggggt gggcgtgcac 1260
ttctcgccgg gggcccgggc gctcaccaca cctgcagtgc atgtcaatgg ccttgaacct 1320

tatgccaact acacctttaa tgtggaagcc caaaatggag tgtcagggct gggcagctct 1380
ggccatgcca gcacctcagt cagcatcagc atggggcatg cagagtcact gtcaggcctg 1440
tctctgagac tggtgaagaa agaaccgagg caactagagc tgacctgggc ggggtcccgg 1500
ccccgaagcc ctggggcgaa cctgacctat gagctgcacg tgctgaacca ggatgaagaa 1560
cggtaccaga tggttctaga acccagggtc ttgctgacag agctgcagcc tgacaccaca 1620
tacatcgtca gagtccgaat gctgacccca ctgggtcctg gccctttctc ccctgatcat 1680
gagtttcgga ccagcccacc agtgtccagg ggcctgactg gaggagagat tgtagccgtc 1740
atctttgggc tgctgcttgg tgcagccttg ctgcttggga ttctcgtttt ccggtccagg 1800
agagcccagc ggcagaggca gcagaggcag cgtgaccgcg ccaccgatgt ggatcgagag 1860
gacaagctgt ggctgaagcc ttatgtggac ctccaggcat acgaggaccc tgcacaggga 1920
gccttggact ttacccggga gcttgatcca gcgtggctga tggtggacac tgtcatagga 1980
gaaggagagt ttggggaagt gtatcgaggg accctgaggc tccccagcca ggactgcaag 2040
actgtggcca ttaagacctt aaaagacaca tccccaggtg gccagtggtg gaacttcctt 2100
cgagaggcaa ctatcatggg ccagtttagc cacccgcata ttctgcatct ggaaggcgtc 2160
gtcacaaagc gaaagccgat catgatcatc acagaattta tggagaatgg agccctggat 2220
gccttcctga gggagcggga ggaccagctg gtccctgggc agctagtggc catgctgcag 2280
ggcatagcat ctggcatgaa ctacctcagt aatcacaatt atgtccaccg ggacctggct 2340
gccagaaaca tcttggtgaa tcaaaacctg tgctgcaagg tgtctgactt tggcctgact 2400
cgcctcctgg atgactttga tggcacatac gaaacccagg gaggaaagat ccctatccgt 2460
tggacagccc ctgaagccat tgcccatcgg atcttcacca cagccagcga tgtgtggagc 2520
tttgggattg tgatgtggga ggtgctgagc tttggggaca agccttatgg ggagatgagc 2580
aatcaggagg ttatgaagag cattgaggat gggtaccggt tgcccccctcc tgtggactgc 2640
cctgcccctc tgtatgagct catgaagaac tgctgggcat atgaccgtgc ccgccggcca 2700
cacttccaga agcttcaggc acatctggag caactgcttg ccaaccccca ctccctgcgg 2760
accattgcca actttgaccc cagggtgact cttcgcctgc ccagcctgag tggctcagat 2820
gggatcccgt atcgaaccgt ctctgagtgg ctcgagtcca tacgcatgaa acgctacatc 2880
ctgcacttcc actcggctgg gctggacacc atggagtgtg tgctggagct gaccgctgag 2940
gacctgacgc agatgggaat cacactgccc gggcaccaga agcgcattct ttgcagtatt 3000
cagggattca aggactgatc cctcctctca ccccatgccc aatcagggtg caaggagcaa 3060
ggacggggcc aaggtcgctc atggtcactc cctgcgcccc ttcccacaac ctgccagact 3120
aggctatcgg tgctgcttct gcccactttc aggagaaccc tgctctgcac cccagaaaac 3180
ctctttgttt taaaagggag gtgggggtag aagtaaaagg atgatcatgg gagggagctg 3240
aggggttaat atatatacat acatacacat atatatattt ttgtaaataa acaggaactg 3300
attttctgcc tccatcccac ccatgagggc tgcaggcact acaaaagagc tgactactga 3360
gaa 3363

<210> 166
<211> 3865
<212> DNA
<213> Homo Sapiens

<300>
<308> GenBank No. NM004441
<309> 2004-11-15

<400> 166
cacatgcaca cccacaccca cgcgcgcccg caccgcccca cgcgcacaca ctcctgccca 60
cgcccacgca gcgctccggg aagtccggtc cgggcgagag cgcgaaagga taccgagaag 120
ccacccgcgg agagcgcagc ggcgccctgg gacgcggcgc tctcccggcg ctgctgcctc 180
ggcttggtct cggcctgcgg gccgtcggcc ggcgatggcc ctggattatc tactactgct 240
cctcctggca tccgcagtgg ctgcgatgga agaaacgtta atggacacca gaacggctac 300
tgcagagctg ggctggacgg ccaatcctgc gtccgggtgg gaagaagtca gtggctacga 360
tgaaaacctg aacaccatcc gcacctacca ggtgtgcaat gtcttcgagc ccaaccagaa 420
caattggctg ctcaccacct tcatcaaccg gcgggggccc catcgcatct acacagagat 480
gcgcttcact gtgagagact gcagcagcct ccctaatgtc ccaggatcct gcaaggagac 540
cttcaacttg tattactatg agactgactc tgtcattgcc accaagaagt cagccttctg 600

gtctgaggcc ccctacctca aagtagacac cattgctgca gatgagagct tctcccaggt 660
ggactttggg ggaaggctga tgaaggtaaa cacagaagtc aggagctttg ggcctcttac 720
tcggaatggt ttttacctcg cttttcagga ttatggagcc tgtatgtctc ttctttctgt 780
ccgtgtcttc ttcaaaaagt gtcccagcat tgtgcaaaat tttgcagtgt ttccagagac 840
tatgacaggg gcagagagca catctctggt gattgctcgg ggcacatgca tccccaacgc 900
agaggaagtg gacgtgccca tcaaactcta ctgcaacggg gatggggaat ggatggtgcc 960
tattgggcga tgcacctgca agcctggcta tgagcctgag aacagcgtgg catgcaaggc 1020
ttgccctgca gggacattca aggccagcca ggaagctgaa ggctgctccc actgcccctc 1080
caacagccgc tcccctgcag aggcgtctcc catctgcacc tgtcggaccg gttattaccg 1140
agcggacttt gaccctccag aagtggcatg cactagcgtc ccatcaggtc cccgcaatgt 1200
tatctccatc gtcaatgaga cgtccatcat tctggagtgg caccctccaa gggagacagg 1260
tgggcgggat gatgtgacct acaacatcat ctgcaaaaag tgccgggcag accgccggag 1320
ctgctcccgc tgtgacgaca atgtggagtt tgtgcccagg cagctgggcc tgacggagtg 1380
ccgcgtctcc atcagcagcc tgtgggccca cacccctac acctttgaca tccaggccat 1440
caatggagtc tccagcaaga gtcccttccc cccacagcac gtctctgtca acatcaccac 1500
aaaccaagcc gccccctcca ccgttcccat catgcaccaa gtcagtgcca ctatgaggag 1560
catcaccttg tcatggccac agccggagca gcccaatggc atcatcctgg actatgagat 1620
ccggtactat gagaaggaac acaatgagtt caactcctcc atggccagga gtcagaccaa 1680
cacagcaagg attgatgggc tgcggcctgg catggtatat gtggtacagg tgcgtgcccg 1740
cactgttgct ggctacggca agttcagtgg caagatgtgc ttccagactc tgactgacga 1800
tgattacaag tcagagctga gggagcagct gcccctgatt gctggctcgg cagcggccgg 1860
ggtcgtgttc gttgtgtcct tggtggccat ctctatcgtc tgtagcagga aacgggctta 1920
tagcaaagag gctgtgtaca gcgataagct ccagcattac agcacaggcc gaggctcccc 1980
agggatgaag atctacattg acccccttcac ttatgaggat cccaacgaag ctgtccggga 2040
gtttgccaag gagattgatg tatcttttgt gaaaattgaa gaggtcatcg gagcagggga 2100
gtttggagaa gtgtacaagg ggcgtttgaa actgccaggc aagagggaaa tctacgtggc 2160
catcaagacc ctgaaggcag ggtactcgga gaagcagcgt cgggactttc tgagtgaggc 2220
gagcatcatg ggccagttcg accatcctaa catcattcgc ctggagggtg tggtcaccaa 2280
gagtcggcct gtcatgatca tcacagagtt catggagaat ggtgcattgg attctttcct 2340
caggcaaaat gacgggcagt tcaccgtgat ccagcttgtg ggtatgctca ggggcatcgc 2400
tgctggcatg aagtacctgg ctgagatgaa ttatgtgcat cgggacctgg ctgctaggaa 2460
cattctggtc aacagtaacc tggtgtgcaa ggtgtccgac tttggcctct cccgctacct 2520
ccaggatgac acctcagatc ccacctacac cagctccttg ggagggaaga tccctgtgag 2580
atggacagct ccagaggcca tcgcctaccg caagttcact tcagccagcg acgtttggag 2640
ctatgggatc gtcatgtggg aagtcatgtc atttggagag agaccctatt gggatatgtc 2700
caaccaagat gtcatcaatg ccatcgagca ggactaccgg ctgcccccac ccatggactg 2760
tccagctgct ctacaccagc tcatgctgga ctgttggcag aaggaccgga acagccggcc 2820
ccggtttgcg gagattgtca acaccctaga taagatgatc cggaacccgg caagtctcaa 2880
gactgtggca accatcaccg ccgtgccttc ccagcccctg ctcgaccgct ccatcccaga 2940
cttcacggcc tttaccaccg tggatgactg gctcagcgcc atcaaaatgg tccagtacag 3000
ggacagcttc ctcactgctg gcttcacctc cctccagctg gtcacccaga tgacatcaga 3060
agacctcctg agaataggca tcaccttggc aggccatcag aagaagatcc tgaacagcat 3120
tcattctatg agggtccaga taagtcagtc accaacggca atggcatgag aactcttgtt 3180
tcttggggaa ggagaggagg gaaaaggacc agggtcaagg gggaccagag gttgaccact 3240
gtggaatgta ctggagagac tggcttctca gctgaggaat gcatttccat cagtgaagaa 3300
tcaaccggac ctgttgctag caggcaatct ccatttctca gtgacagaag catgtttgag 3360
atgccgtggg aaaccaaata tataataata aaaatataaa aaggtgatgt tcaacagaag 3420
tgaagacaaa acaatatgca tcaggagaac aagagtaaac ccagctccca ctctcagtgg 3480
gctgcagttg cccaaccaca ggaagaaagg gaaggaggta gagggaagaa acagaagcag 3540
tgttccattt tcttcctcac caatgacatt cttttctttt ctcctttcgt actcctccct 3600
gagagtcccc tcccttctcc cacactcgtt tcccctttgct catgactcct gtagggaagt 3660
ttcttcaaac aaaacccagc tcctgagtct ccagatgttg ttctgtcagt tgccaaagga 3720
ctttgctgac cactgcatgg ggatccaacc aattcaatta atgtcttcat attgaagaag 3780
agatgtacct tcaattgaaa acctcgtttt tcttttgttt gcattttctg caaaaaggaa 3840
aaagaaacca caaattgggg aattc 3865

<210> 167
<211> 1721
<212> DNA
<213> Homo Sapiens

<400> 167
ctctctggct actagagacc cactgcttac tggcttatcg aaattaatac gactcactat 60
agggagaccc aagctggcta gttaagcttg gtaccgagct cggatccacc atggagctcc 120
aggcagcccg cgcctgcttc gccctgctgt ggggctgtgc gctggccgcg gccgcggcgg 180
cgcagggcaa ggaagtggta ctgctggact ttgctgcagc tggaggggag ctcggctggc 240
tcacacaccc gtatggcaaa gggtgggacc tgatgcagaa catcatgaat gacatgccga 300
tctacatgta ctccgtgtgc aacgtgatgt ctggcgacca ggacaactgg ctccgcacca 360
actgggtgta ccgaggagag gctgagcgta tcttcattga gctcaagttt actgtacgtg 420
actgcaacag cttccctggt ggcgccagct cctgcaagga gactttcaac ctctactatg 480
ccgagtcgga cctggactac ggcaccaact tccagaagcg cctgttcacc aagattgaca 540
ccattgcgcc cgatgagatc accgtcagca gcgacttcga ggcacgccac gtgaagctga 600
acgtggagga gcgctccgtg gggccgctca cccgcaaagg cttctacctg gccttccagg 660
atatcggtgc ctgtgtggca ctactctccg tccgtgtcta ctacgagaag tgccccgagc 720
cgctgcaggg cctggcccac ttccctgaga ccatcgccgg ctctgatgca ccttccctgg 780
ccactgtggc cggcacctgt gtggaccatg ccgtggtgcc accggggggt gaagagcccc 840
gtatgcactg tgcagtggat ggcgagtggc tggtgcccat tgggcagtgc ctgtgccagg 900
caggctacga gaaggtggag gatgcctgcc aggcctgctc gcctggattt tttaagtttg 960
aggcatccga gagcccctgc ttggagtgcc ctgagcgcac gctgccatcc cctgagggtg 1020
ccacctcctg cgagtgtgag gaaggcttct tccgggcacc tcaggaccca gcgtcgatgc 1080
cttgcacacg acccccttcc gccccacact acctcacagc cgtgggcatg ggtgccaagg 1140
tggagctgcg ctggacgccc cctcaggaca gcgggggccg cgaggacatt gtctacagcg 1200
tcacctgcga acagtgctgg cccgagtctg gggaatgcgg gccgtgtgag gccagtgtgc 1260
gctactcgga gcctcctcac ggactgaccc gcaccagtgt gacagtgagc gacctggagc 1320
cccacatgaa ctacaccttc accgtggagg cccgcaatgg cgtctcaggc ctggtaacca 1380
gccgcagctt ccgtactgcc agtgtcagca tcaaccagac agagcccccc aaggtgaggc 1440
tggagggccg cagcaccacc tcgcttagcg tctcctggag catccccccg ccgcagcaga 1500
gccgagtgtg gaagtacgag gtcacttacc gcaagaaggt aactcccaga ggggcggggc 1560
tggctctagc tgggccgaca gcaggggaca ggctggtcac actcgagtct agagggccct 1620
tcgaacaaaa actcatctca gaagaggatc tgaatatgca taccggtcat catcaccatc 1680
accattgagt ttaaacccgc tgatcagcct cgactgtgcc t 1721

<210> 168
<211> 497
<212> PRT
<213> Homo Sapiens

<400> 168
Met Glu Leu Gln Ala Ala Arg Ala Cys Phe Ala Leu Leu Trp Gly Cys
 1 5 10 15
Ala Leu Ala Ala Ala Ala Ala Ala Gln Gly Lys Glu Val Val Leu Leu
 20 25 30
Asp Phe Ala Ala Ala Gly Gly Glu Leu Gly Trp Leu Thr His Pro Tyr
 35 40 45
Gly Lys Gly Trp Asp Leu Met Gln Asn Ile Met Asn Asp Met Pro Ile
 50 55 60
Tyr Met Tyr Ser Val Cys Asn Val Met Ser Gly Asp Gln Asp Asn Trp
65 70 75 80
Leu Arg Thr Asn Trp Val Tyr Arg Gly Glu Ala Glu Arg Ile Phe Ile
 85 90 95
Glu Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Phe Pro Gly Gly Ala

```
            100                 105                 110
Ser Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Ala Glu Ser Asp Leu
        115                 120                 125
Asp Tyr Gly Thr Asn Phe Gln Lys Arg Leu Phe Thr Lys Ile Asp Thr
    130                 135                 140
Ile Ala Pro Asp Glu Ile Thr Val Ser Ser Asp Phe Glu Ala Arg His
145                 150                 155                 160
Val Lys Leu Asn Val Glu Glu Arg Ser Val Gly Pro Leu Thr Arg Lys
                165                 170                 175
Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Val Ala Leu Leu
            180                 185                 190
Ser Val Arg Val Tyr Tyr Glu Lys Cys Pro Glu Pro Leu Gln Gly Leu
        195                 200                 205
Ala His Phe Pro Glu Thr Ile Ala Gly Ser Asp Ala Pro Ser Leu Ala
    210                 215                 220
Thr Val Ala Gly Thr Cys Val Asp His Ala Val Val Pro Pro Gly Gly
225                 230                 235                 240
Glu Glu Pro Arg Met His Cys Ala Val Asp Gly Glu Trp Leu Val Pro
                245                 250                 255
Ile Gly Gln Cys Leu Cys Gln Ala Gly Tyr Glu Lys Val Glu Asp Ala
            260                 265                 270
Cys Gln Ala Cys Ser Pro Gly Phe Phe Lys Phe Glu Ala Ser Glu Ser
        275                 280                 285
Pro Cys Leu Glu Cys Pro Glu Arg Thr Leu Pro Ser Pro Glu Gly Ala
    290                 295                 300
Thr Ser Cys Glu Cys Glu Glu Gly Phe Phe Arg Ala Pro Gln Asp Pro
305                 310                 315                 320
Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro His Tyr Leu Thr
                325                 330                 335
Ala Val Gly Met Gly Ala Lys Val Glu Leu Arg Trp Thr Pro Pro Gln
            340                 345                 350
Asp Ser Gly Gly Arg Glu Asp Ile Val Tyr Ser Val Thr Cys Glu Gln
        355                 360                 365
Cys Trp Pro Glu Ser Gly Glu Cys Gly Pro Cys Glu Ala Ser Val Arg
    370                 375                 380
Tyr Ser Glu Pro Pro His Gly Leu Thr Arg Thr Ser Val Thr Val Ser
385                 390                 395                 400
Asp Leu Glu Pro His Met Asn Tyr Thr Phe Thr Val Glu Ala Arg Asn
                405                 410                 415
Gly Val Ser Gly Leu Val Thr Ser Arg Ser Phe Arg Thr Ala Ser Val
            420                 425                 430
Ser Ile Asn Gln Thr Glu Pro Pro Lys Val Arg Leu Glu Gly Arg Ser
        435                 440                 445
Thr Thr Ser Leu Ser Val Ser Trp Ser Ile Pro Pro Pro Gln Gln Ser
    450                 455                 460
Arg Val Trp Lys Tyr Glu Val Thr Tyr Arg Lys Lys Val Thr Pro Arg
465                 470                 475                 480
Gly Ala Gly Leu Ala Leu Ala Gly Pro Thr Ala Gly Asp Arg Leu Val
                485                 490                 495
Thr
```

<210> 169
<211> 1353
<212> DNA
<213> Homo Sapiens

<400> 169
agtcccgcgc ggagtatcgg cgtccacccg cccagggaga gtcagacctg ggggggcgag 60
ggcccccaa actcagttcg gatcctaccc gagtgaggcg gcgccatgga gctccgggtg 120
ctgctctgct gggcttcgtt ggccgcagct ttggaagaga ccctgctgaa cacaaaattg 180
gaaactgctg atctgaagtg ggtgacattc cctcaggtgg acgggcagtg ggaggaactg 240
agcggcctgg atgaggaaca gcacagcgtg cgcacctacg aagtgtgtga cgtgcagcgt 300
gccccgggcc aggcccactg gcttcgcaca ggttgggtcc cacggcgggg cgccgtccac 360
gtgtacgcca cgctgcgctt caccatgctc gagtgcctgt ccctgcctcg ggctgggcgc 420
tcctgcaagg agaccttcac cgtcttctac tatgagagcg atgcggacac ggccacggcc 480
ctcacgccag cctggatgga gaacccctac atcaaggtgg acacggtggc cgcggagcat 540
ctcacccgga agcgccctgg ggccgaggcc accgggaagg tgaatgtcaa gacgctgcgt 600
ctgggaccgc tcagcaaggc tggcttctac ctggccttcc aggaccaggg tgcctgcatg 660
gccctgctat ccctgcacct cttctacaaa aagtgcgccc agctgactgt gaacctgact 720
cgattcccgg agactgtgcc tcgggagctg gttgtgcccg tggccggtag ctgcgtggtg 780
gatgccgtcc ccgcccctgg ccccagcccc agcctctact gccgtgagga tggccagtgg 840
gccgaacagc cggtcacggg ctgcagctgt gctccggggt tcgaggcagc tgaggggaac 900
accaagtgcc gagggcgccg agggtcccag cagcgtgcgg ttcctgaaga cgtcagaaaa 960
ccgggcagag ctgcgggggc tgaagcgggg agccagctac ctggtgcagg tacgggcgcg 1020
ctctgaggcc ggctacgggc ccttcggcca ggaacatcac agccagaccc aactggatga 1080
gagcgagggc tggcgggagc agctggccct gattgcgggc acggcagtcg tgggtgtggt 1140
cctggtcctg gtggtcattg tggtcgcagt tctctgcctc aggaagcaga gcaatgggag 1200
agaagcagaa tattcggaca aacacggaca gtatctcatc ggacatggta ctaaggtcta 1260
catcgacccc ttcacttatg aagaccctaa tgaggctgtg agggaatttg caaaagagat 1320
cgatgtctcc tacgtcaaga ttgaagaggt gat 1353

<210> 170
<211> 306
<212> PRT
<213> Homo Sapiens

<400> 170
Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
 1   5   10   15
Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
            20   25   30
Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
        35   40   45
Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
    50   55   60
Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65   70   75   80
Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
                85   90   95
Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
            100   105   110
Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
        115   120   125
Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
    130   135   140
His Leu Thr Arg Lys Arg Pro Gly Ala Glu Ala Thr Gly Lys Val Asn
145   150   155   160
Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
                165   170   175
Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
            180   185   190

```
Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
        195                 200                 205
Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
    210                 215                 220
Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225                 230                 235                 240
Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
                245                 250                 255
Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Gly Arg Arg
            260                 265                 270
Gly Ser Gln Gln Arg Ala Val Pro Glu Asp Val Arg Lys Pro Gly Arg
        275                 280                 285
Ala Ala Gly Ala Glu Ala Gly Ser Gln Leu Pro Gly Ala Gly Thr Gly
    290                 295                 300
Ala Leu
305
```

<210> 171
<211> 1813
<212> DNA
<213> Homo Sapiens

<400> 171

```
actcagttcg gatcctaccc gagtgaggcg gcgccatgga gctccgggtg ctgctctgct 60
gggcttcgtt ggccgcagct ttggaagaga ccctgctgaa cacaaaattg gaaactgctg 120
atctgaagtg ggtgacattc cctcaggtgg acgggcagtg ggaggaactg agcggcctgg 180
atgaggaaca gcacagcgtg cgcacctacg aagtgtgtga cgtgcagcgt gccccgggcc 240
aggcccactg gcttcgcaca ggttgggtcc cacggcgggg cgccgtccac gtgtacgcca 300
cgctgcgctt caccatgctc gagtgcctgt ccctgcctcg ggctgggcgc tcctgcaagg 360
agaccttcac cgtcttctac tatgagagcg atgcggacac ggccacggcc ctcacgccag 420
cctggatgga gaacccctac atcaaggtgg acacggtggc cgcggagcat ctcacccgga 480
agcgccctgg ggccgaggcc accgggaagg tgaatgtcaa gacgctgcgt ctgggaccgc 540
tcagcaaggc tggcttctac ctggccttcc aggaccaggg tgcctgcatg gccctgctat 600
ccctgcacct cttctacaaa aagtgcgccc agctgactgt gaacctgact cgattcccgg 660
agactgtgcc tcgggagctg gttgtgcccg tggccggtag ctgcgtggtg gatgccgtcc 720
ccgcccctgg ccccagcccc agcctctact gccgtgagga tggccagtgg gccgaacagc 780
cggtcacggg ctgcagctgt gctccggggt tcgaggcagc tgaggggaac accaagtgcc 840
gagcctgtgc ccagggcacc ttcaagcccc tgtcaggaga agggtcctgc cagccatgcc 900
cagccaatag ccactctaac accattggat cagccgtctg ccagtgccgc gtcgggtact 960
tccgggcacg cacagacccc cggggtgcac cctgcaccac ccctccttcg gctccgcgga 1020
gcgtggtttc ccgcctgaac ggctcctccc tgcacctgga atggagtgcc cccctggagt 1080
ctggtggccg agaggacctc acctacgccc tccgctgccg ggagtgccga cccggaggct 1140
cctgtgcgcc ctgcgggggа gacctgactt ttgaccccgg cccccgggac ctggtggagc 1200
cctgggtggt ggttcgaggg ctacgtcctg acttcaccta tacctttgag gtcactgcat 1260
tgaacggggt atcctcctta gccacggggc ccgtcccatt tgagcctgtc aatgtcacca 1320
ctgaccgaga ggtacctcct gcagtgtctg acatccgggt gacgcggtcc tcacccagca 1380
gcttgagcct ggcctgggct gttccccggg cacccagtgg ggctgtgctg gactacgagg 1440
tcaaatacca tgagaagggc gccgagggtc ccagcagcgt gcggttcctg aagacgtcag 1500
aaaaccgggc agagctgcgg gggctgaagc ggggagccag ctacctggtg cagagagcga 1560
gggctggcgg gagcagctgg ccctgattgc gggcacggca gtcgtgggtg tggtcctggt 1620
cctggtggtc attgtggtcg cagttctctg cctcaggaag cagagcaatg ggagagaagc 1680
agaatattcg gacaaacacg gacagtatct catcggacat ggtactaagg tctacatcga 1740
ccccttcact tatgaagacc ctaatgaggc tgtgagggaa tttgcaaaag agatcgatgt 1800
ctcctacgtc aag                                                    1813
```

<210> 172
<211> 516
<212> PRT
<213> Homo Sapiens

<400> 172
Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
1 5 10 15
Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
20 25 30
Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
35 40 45
Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
50 55 60
Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65 70 75 80
Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
85 90 95
Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
100 105 110
Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
115 120 125
Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
130 135 140
His Leu Thr Arg Lys Arg Pro Gly Ala Glu Ala Thr Gly Lys Val Asn
145 150 155 160
Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
165 170 175
Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
180 185 190
Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
195 200 205
Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
210 215 220
Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225 230 235 240
Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
245 250 255
Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Ala Cys Ala
260 265 270
Gln Gly Thr Phe Lys Pro Leu Ser Gly Glu Gly Ser Cys Gln Pro Cys
275 280 285
Pro Ala Asn Ser His Ser Asn Thr Ile Gly Ser Ala Val Cys Gln Cys
290 295 300
Arg Val Gly Tyr Phe Arg Ala Arg Thr Asp Pro Arg Gly Ala Pro Cys
305 310 315 320
Thr Thr Pro Pro Ser Ala Pro Arg Ser Val Val Ser Arg Leu Asn Gly
325 330 335
Ser Ser Leu His Leu Glu Trp Ser Ala Pro Leu Glu Ser Gly Gly Arg
340 345 350
Glu Asp Leu Thr Tyr Ala Leu Arg Cys Arg Glu Cys Arg Pro Gly Gly
355 360 365
Ser Cys Ala Pro Cys Gly Gly Asp Leu Thr Phe Asp Pro Gly Pro Arg
370 375 380
Asp Leu Val Glu Pro Trp Val Val Val Arg Gly Leu Arg Pro Asp Phe
385 390 395 400

```
Thr Tyr Thr Phe Glu Val Thr Ala Leu Asn Gly Val Ser Ser Leu Ala
                405                 410                 415
Thr Gly Pro Val Pro Phe Glu Pro Val Asn Val Thr Thr Asp Arg Glu
            420                 425                 430
Val Pro Pro Ala Val Ser Asp Ile Arg Val Thr Arg Ser Ser Pro Ser
        435                 440                 445
Ser Leu Ser Leu Ala Trp Ala Val Pro Arg Ala Pro Ser Gly Ala Val
    450                 455                 460
Leu Asp Tyr Glu Val Lys Tyr His Glu Lys Gly Ala Glu Gly Pro Ser
465                 470                 475                 480
Ser Val Arg Phe Leu Lys Thr Ser Glu Asn Arg Ala Glu Leu Arg Gly
                485                 490                 495
Leu Lys Arg Gly Ala Ser Tyr Leu Val Gln Arg Ala Arg Ala Gly Gly
            500                 505                 510
Ser Ser Trp Pro
        515
```

<210> 173
<211> 1801
<212> DNA
<213> Homo Sapiens

<400> 173

```
actcagttcg gatcctaccc gagtgaggcg gcgccatgga gctccgggtg ctgctctgct 60
gggcttcgtt ggccgcagct ttggaagaga ccctgctgaa cacaaaattg gaaactgctg 120
atctgaagtg ggtgacattc cctcaggtgg acgggcagtg ggaggaactg agcggcctgg 180
atgaggaaca gcacagcgtg cgcacctacg aagtgtgtga cgtgcagcgt gccccgggcc 240
aggcccactg gcttcgcaca ggttgggtcc cacggcgggg cgccgtccac gtgtacgcca 300
cgctgcgctt caccatgctc gagtgcctgt ccctgcctcg ggctgggcgc tcctgcaagg 360
agaccttcac cgtcttctac tatgagagcg atgcggacac ggccacggcc ctcacgccag 420
cctggatgga gaacccctac atcaaggtgg acacggtggc cgcggagcat ctcacccgga 480
agcgccctgg ggccgaggcc accgggaagg tgaatgtcaa gacgctgcgt ctgggaccgc 540
tcagcaaggc tggcttctac ctggccttcc aggaccaggg tgcctgcatg gccctgctat 600
ccctgcacct cttctacaaa aagtgcgccc agctgactgt gaacctgact cgattcccgg 660
agactgtgcc tcgggagctg gttgtgcccg tggccggtag ctgcgtggtg gatgccgtcc 720
ccgcccctgg ccccagcccc agcctctact gccgtgagga tggccagtgg gccgaacagc 780
cggtcacggg ctgcagctgt gctccggggt tcgaggcagc tgaggggaac accaagtgcc 840
gagcctgtgc ccagggcacc ttcaagcccc tgtcaggaga agggtcctgc cagccatgcc 900
cagccaatag ccactctaac accattggat cagccgtctg ccagtgccgc gtcgggtact 960
tccgggcacg cacagacccc cggggtgcac cctgcaccac ccctccttcg gctccgcgga 1020
gcgtggtttc ccgcctgaac ggctcctccc tgcacctgga atggagtgcc cccctggagt 1080
ctggtggccg agaggacctc acctacgccc tccgctgccg ggagtgccga cccggaggct 1140
cctgtgcgcc ctgcgggggga gacctgactt ttgaccccgg cccccgggac ctggtggagc 1200
cctgggtggt ggttcgaggg ctacgtcctg acttcaccta taccttgag tacctcctgc 1260
agtgtctgac atccgggtga cgcggtcctc acccagcagc ttgagcctgg cctgggctgt 1320
tccccgggca cccagtgggg ctgtgctgga ctacgaggtc aaataccatg agaagggcgc 1380
cgagggtccc agcagcgtgc ggttcctgaa gacgtcagaa aaccgggcag agctgcgggg 1440
gctgaagcgg ggagccagct acctggtgca ggtacgggcg cgctctgagg ccggctacgg 1500
gcccttcggc caggaacatc acagccagac ccaactggat gagagcgagg gctggcggga 1560
gcagctggcc ctgattgcgg gcacggcagt cgtgggtgtg gtcctggtcc tggtggtcat 1620
tgtggtcgca gttctctgcc tcaggaagca gagcaatggg agagaagcag aatattcgga 1680
caaacacgga cagtatctca tcggacatgg tactaaggtc tacatcgacc ccttcactta 1740
tgaagaccct aatgaggctg tgagggaatt tgcaaaagag atcgatgtct cctacgtcaa 1800
g                                                                  1801
```

<210> 174
<211> 414
<212> PRT
<213> Homo Sapiens

<400> 174
Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
1 5 10 15
Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
20 25 30
Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
35 40 45
Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
50 55 60
Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65 70 75 80
Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
85 90 95
Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
100 105 110
Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
115 120 125
Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
130 135 140
His Leu Thr Arg Lys Arg Pro Gly Ala Glu Ala Thr Gly Lys Val Asn
145 150 155 160
Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
165 170 175
Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
180 185 190
Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
195 200 205
Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
210 215 220
Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225 230 235 240
Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
245 250 255
Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Ala Cys Ala
260 265 270
Gln Gly Thr Phe Lys Pro Leu Ser Gly Glu Gly Ser Cys Gln Pro Cys
275 280 285
Pro Ala Asn Ser His Ser Asn Thr Ile Gly Ser Ala Val Cys Gln Cys
290 295 300
Arg Val Gly Tyr Phe Arg Ala Arg Thr Asp Pro Arg Gly Ala Pro Cys
305 310 315 320
Thr Thr Pro Pro Ser Ala Pro Arg Ser Val Val Ser Arg Leu Asn Gly
325 330 335
Ser Ser Leu His Leu Glu Trp Ser Ala Pro Leu Glu Ser Gly Gly Arg
340 345 350
Glu Asp Leu Thr Tyr Ala Leu Arg Cys Arg Glu Cys Arg Pro Gly Gly
355 360 365
Ser Cys Ala Pro Cys Gly Gly Asp Leu Thr Phe Asp Pro Gly Pro Arg
370 375 380
Asp Leu Val Glu Pro Trp Val Val Val Arg Gly Leu Arg Pro Asp Phe
385 390 395 400

```
Thr Tyr Thr Phe Glu Tyr Leu Leu Gln Cys Leu Thr Ser Gly
                405                 410
```

<210> 175
<211> 965
<212> DNA
<213> Homo Sapiens

<400> 175
atgtggagct ggaagtgcct cctcttctgg gctgtgctgg tcacagccac actctgcacc 60
gctaggccgt ccccgacctt gcctgaacaa gatgctctcc cctcctcgga ggatgatgat 120
gatgatgatg actcctcttc agaggagaaa gaaacagata acaccaaacc aaaccgtatg 180
cccgtagctc catattggac atccccagaa aagatggaaa agaaattgca tgcagtgccg 240
gctgccaaga cagtgaagtt caaatgccct tccagtggga ccccaaaccc cacactgcgc 300
tggttggaaa atggcaaaga attcaaacct ggccacagaa ttggaggcta caaggtccgt 360
tatgccacct ggagcatcat aatggactct gtggtgccct ctgacaaggg caactacacc 420
tgcattgtgg agaatgagta cggcagcatc aaccacacat accagctgga tgtcgtggag 480
cggtcccctc accggcccat cctgcaagca gggttgcccg ccaacaaaac agtggccctg 540
ggtagcaacg tggagttcat gtgtaaggtg tacagtgacc cgcagccgca catccagtgg 600
ctaaagcaca tcgaggtgaa tgggagcaag attggcccgg acaacctgcc ttatgtccag 660
atcttgaaga ctgctggagt taataccacc gacaaagaga tggaggtgct tcacttaaga 720
aatgtctcct ttgaggacgc aggggagtat acgtgcttgg cgggtaactc tatcggactc 780
tcccatcact ctgcatggtt gaccgttctg gaaggtacac actgtaactt ctcctctcga 840
tgtcctgccc tcgccacggg cacgggggga gcatgcattt ccaggcttgg ggagacacag 900
aggcaggaga gctggaagaa tgggctcctg cctgcctggt gccacatcct gccccagctt 960
tgagg 965

<210> 176
<211> 320
<212> PRT
<213> Homo Sapiens

<400> 176
```
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
 1               5                  10                  15
Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Asp Ala
            20                  25                  30
Leu Pro Ser Ser Glu Asp Asp Asp Asp Asp Asp Asp Ser Ser Ser Glu
        35                  40                  45
Glu Lys Glu Thr Asp Asn Thr Lys Pro Asn Arg Met Pro Val Ala Pro
    50                  55                  60
Tyr Trp Thr Ser Pro Glu Lys Met Glu Lys Lys Leu His Ala Val Pro
65                  70                  75                  80
Ala Ala Lys Thr Val Lys Phe Lys Cys Pro Ser Ser Gly Thr Pro Asn
                85                  90                  95
Pro Thr Leu Arg Trp Leu Glu Asn Gly Lys Glu Phe Lys Pro Gly His
            100                 105                 110
Arg Ile Gly Gly Tyr Lys Val Arg Tyr Ala Thr Trp Ser Ile Ile Met
        115                 120                 125
Asp Ser Val Val Pro Ser Asp Lys Gly Asn Tyr Thr Cys Ile Val Glu
    130                 135                 140
Asn Glu Tyr Gly Ser Ile Asn His Thr Tyr Gln Leu Asp Val Val Glu
145                 150                 155                 160
Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro Ala Asn Lys
                165                 170                 175
```

```
Thr Val Ala Leu Gly Ser Asn Val Glu Phe Met Cys Lys Val Tyr Ser
            180                 185                 190
Asp Pro Gln Pro His Ile Gln Trp Leu Lys His Ile Glu Val Asn Gly
        195                 200                 205
Ser Lys Ile Gly Pro Asp Asn Leu Pro Tyr Val Gln Ile Leu Lys Thr
    210                 215                 220
Ala Gly Val Asn Thr Thr Asp Lys Glu Met Glu Val Leu His Leu Arg
225                 230                 235                 240
Asn Val Ser Phe Glu Asp Ala Gly Glu Tyr Thr Cys Leu Ala Gly Asn
                245                 250                 255
Ser Ile Gly Leu Ser His His Ser Ala Trp Leu Thr Val Leu Glu Gly
            260                 265                 270
Thr His Cys Asn Phe Ser Ser Arg Cys Pro Ala Leu Ala Thr Gly Thr
        275                 280                 285
Gly Gly Ala Cys Ile Ser Arg Leu Gly Glu Thr Gln Arg Gln Glu Ser
    290                 295                 300
Trp Lys Asn Gly Leu Leu Pro Ala Trp Cys His Ile Leu Pro Gln Leu
305                 310                 315                 320
```

<210> 177
<211> 801
<212> DNA
<213> Homo Sapiens

<400> 177

```
atggtcagct ggggtcgttt catctgcctg gtcgtggtca ccatggcaac cttgtccctg 60
gcccggccct ccttcagttt agttgaggat accacattag agccagaaga gccaccaacc 120
aaataccaaa tctctcaacc agaagtgtac gtggctgcgc caggggagtc gctagaggtg 180
cgctgcctgt tgaaagatgc cgccgtgatc agttggacta aggatggggt gcacttgggg 240
cccaacaata ggacagtgct tattggggag tacttgcaga taaagggcgc cacgcctaga 300
gactccggcc tctatgcttg tactgccagt aggactgtag acagtgaaac ttggtacttc 360
atggtgaatg tcacagatgc catctcatcc ggagatgatg aggatgacac cgatggtgcg 420
gaagattttg tcagtgagaa cagtaacaac aagagagcac catactggac caacacagaa 480
aagatggaaa agcggctcca tgctgtgcct gcggccaaca ctgtcaagtt tcgctgccca 540
gccgggggga acccaatgcc aaccatgcgg tggctgaaaa acgggaagga gtttaagcag 600
gagcatcgca ttggaggcta caaggtacga aaccagcact ggagcctcat tatggaaagt 660
gtggtcccat ctgacaaggg aaattatacc tgtgtggtgg agaatgaata cgggtccatc 720
aatcacacgt accacctgga tgttgtgggt gagtctgcct ctcctcgtgt ggcggctgca 780
taccagccca ttcttgcttg a                                          801
```

<210> 178
<211> 266
<212> PRT
<213> Homo Sapiens

<400> 178

```
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
 1               5                  10                  15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
            20                  25                  30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
        35                  40                  45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
    50                  55                  60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
```

65 70 75 80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
85 90 95
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
100 105 110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
115 120 125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
130 135 140
Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145 150 155 160
Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
165 170 175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
180 185 190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
195 200 205
Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
210 215 220
Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225 230 235 240
Asn His Thr Tyr His Leu Asp Val Val Gly Glu Ser Ala Ser Pro Arg
245 250 255
Val Ala Ala Ala Tyr Gln Pro Ile Leu Ala
260 265

<210> 179
<211> 953
<212> DNA
<213> Homo Sapiens

<400> 179
atggtcagct ggggtcgttt catctgcctg gtcgtggtca ccatggcaac cttgtccctg 60
gcccggccct ccttcagttt agttgaggat accacattag agccagaaga gccaccaacc 120
aaataccaaa tctctcaacc agaagtgtac gtggctgcgc caggggagtc gctagaggtg 180
cgctgcctgt tgaaagatgc cgccgtgatc agttggacta aggatggggt gcacttgggg 240
cccaacaata ggacagtgct tattggggag tacttgcaga taaagggcgc cacgcctaga 300
gactccggcc tctatgcttg tactgccagt aggactgtag acagtgaaac ttggtacttc 360
atggtgaatg tcacagatgc catctcatcc ggagatgatg aggatgacac cgatggtgcg 420
gaagattttg tcagtgagaa cagtaacaac aagagagcac catactggac caacacagaa 480
aagatggaaa agcggctcca tgctgtgcct gcggccaaca ctgtcaagtt tcgctgccca 540
gccgggggga acccaatgcc aaccatgcgg tggctgaaaa acgggaagga gtttaagcag 600
gagcatcgca ttggaggcta caaggtacga aaccagcact ggagcctcat tatggaaagt 660
gtggtcccat ctgacaaggg aaattatacc tgtgtggtgg agaatgaata cgggtccatc 720
aatcacacgt accacctgga tgttgtggag cgatcgcctc accggcccat cctccaagcc 780
ggactgccgg caaatgcctc cacagtggtc ggaggagacg tagagtttgt ctgcaaggtt 840
tacagtgatg cccagcccca catccagtgg atcaagcacg tggaaaagaa cggcagtaaa 900
tacgggcccg acgggctgcc ctacctcaag gttctcaagg tgaggacttt ctg 953

<210> 180
<211> 317
<212> PRT
<213> Homo Sapiens

<400> 180

```
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
 1               5                  10                  15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
            20                  25                  30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
        35                  40                  45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
    50                  55                  60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65                  70                  75                  80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
                85                  90                  95
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
            100                 105                 110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
        115                 120                 125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
    130                 135                 140
Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145                 150                 155                 160
Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
                165                 170                 175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
            180                 185                 190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
        195                 200                 205
Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
    210                 215                 220
Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225                 230                 235                 240
Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
                245                 250                 255
Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
            260                 265                 270
Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
        275                 280                 285
Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
    290                 295                 300
Gly Leu Pro Tyr Leu Lys Val Leu Lys Val Arg Thr Phe
305                 310                 315
```

<210> 181
<211> 844
<212> DNA
<213> Homo Sapiens

<400> 181
atggtcagct ggggtcgttt catctgcctg gtcgtggtca ccatggcaac cttgtccctg 60
gcccggccct ccttcagttt agttgaggat atcacattag agccagaagg agcaccatac 120
tggaccaaca cagaaaagat ggaaaagcgg ctccatgctg tgcctgcggc caacactgtc 180
aagtttcgct gcccagccgg ggggaaccca atgccaacca tgcggtggct gaaaaacggg 240
aaggagttta agcaggagca tcgcattgga ggctacaagg tacgaaacca gcactggagc 300
ctcattatgg aaagtgtggt cccatctgac aagggaaatt atacctgtgt ggtggagaat 360
gaatacgggt ccatcaatca cacgtaccac ctggatgttg tggagcgatc gcctcaccgg 420
cccatcctcc aagccggact gccggcaaat gcctccacag tggtcggagg agacgtagag 480

tttgtctgca aggtttacag tgatgcccag ccccacatcc agtggatcaa gcacgtggaa 540
aagaacggca gtaaatacgg gcccgacggg ctgccctacc tcaaggttct caaggccgcc 600
ggtgttaaca ccacggacaa agagattgag gttctctata ttcggaatgt aacttttgag 660
gacgctgggg aatatacgtg cttggcgggt aattctattg ggatatcctt tcactccgca 720
tggttgacag ttctgccagg tatatactgt tctttctctc tgggtttttt tccttttttct 780
tggttgactg ctataaaatt aacacagctt ctgttatcag aaatggcccc ttttatcctt 840
gcat 844

<210> 182
<211> 281
<212> PRT
<213> Homo Sapiens

<400> 182
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
1 5 10 15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Ile Thr
20 25 30
Leu Glu Pro Glu Gly Ala Pro Tyr Trp Thr Asn Thr Glu Lys Met Glu
35 40 45
Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys Phe Arg Cys
50 55 60
Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu Lys Asn Gly
65 70 75 80
Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys Val Arg Asn
85 90 95
Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser Asp Lys Gly
100 105 110
Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile Asn His Thr
115 120 125
Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile Leu Gln
130 135 140
Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly Asp Val Glu
145 150 155 160
Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Ile
165 170 175
Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp Gly Leu Pro
180 185 190
Tyr Leu Lys Val Leu Lys Ala Ala Gly Val Asn Thr Thr Asp Lys Glu
195 200 205
Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe Glu Asp Ala Gly Glu
210 215 220
Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Ile Ser Phe His Ser Ala
225 230 235 240
Trp Leu Thr Val Leu Pro Gly Ile Tyr Cys Ser Phe Ser Leu Gly Phe
245 250 255
Phe Pro Phe Ser Trp Leu Thr Ala Ile Lys Leu Thr Gln Leu Leu Leu
260 265 270
Ser Glu Met Ala Pro Phe Ile Leu Ala
275 280

<210> 183
<211> 1191
<212> DNA
<213> Homo Sapiens

<400> 183
atggtcagct ggggtcgttt catctgcctg gtcgtggtca ccatggcaac cttgtccctg 60
gcccggccct ccttcagttt agttgaggat accacattag agccagaaga gccaccaacc 120
aaataccaaa tctctcaacc agaagtgtac gtggctgcgc caggggagtc gctagaggtg 180
cgctgcctgt tgaaagatgc cgccgtgatc agttggacta aggatggggt gcacttgggg 240
cccaacaata ggacagtgct tattggggag tacttgcaga taaagggcgc cacgcctaga 300
gactccggcc tctatgcttg tactgccagt aggactgtag acagtgaaac ttggtacttc 360
atggtgaatg tcacagatgc catctcatcc ggagatgatg aggatgacac cgatggtgcg 420
gaagattttg tcagtgagaa cagtaacaac aagagagcac catactggac caacacagaa 480
aagacggaaa agcggctcca tgctgtgcct gcggccaaca ctgtcaagtt tcgctgccca 540
gccgggggga acccaatgcc aaccatgcgg tggctgaaaa acgggaagga gtttaagcag 600
gagcatcgca ttggaggcta caaggtacga aaccagcact ggagcctcat tatggaaagt 660
gtggtcccat ctgacaaggg aaattatacc tgtgtggtgg agaatgaata cgggtccatc 720
aatcacacgt accacctgga tgttgtggag cgatcgcctc accggcccat cctccaagcc 780
ggactgccgg caaatgcctc cacagtggtc ggaggagacg tagagtttgt ctgcaaggtt 840
tacagtgatg cccagcccca catccagtgg atcaagcacg tggaaaagaa cggcagtaaa 900
tacgggcccg acgggctgcc ctacctcaag gttctcaagg ccgccggtgt taacaccacg 960
gacaaagaga ttgaggttct ctatattcgg aatgtaactt ttgaggacgc tggggaatat 1020
acgtgcttgg cgggtaattc tattgggata tcctttcact ctgcatggtt gacagttctg 1080
ccaggtatat actgttcttt ctctctgggt ttttttccct tttcttggtt gactgctata 1140
aaattaacac agcttctgtt atcagaaatg gccccttta tccttgcata a 1191

<210> 184
<211> 396
<212> PRT
<213> Homo Sapiens

<400> 184
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
1 5 10 15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
20 25 30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
35 40 45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
50 55 60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65 70 75 80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
85 90 95
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
100 105 110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
115 120 125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
130 135 140
Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145 150 155 160
Lys Thr Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
165 170 175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
180 185 190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
195 200 205
Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser

```
    210                 215                 220
Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225                 230                 235                 240
Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
                245                 250                 255
Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
            260                 265                 270
Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
        275                 280                 285
Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
    290                 295                 300
Gly Leu Pro Tyr Leu Lys Val Leu Lys Ala Ala Gly Val Asn Thr Thr
305                 310                 315                 320
Asp Lys Glu Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe Glu Asp
                325                 330                 335
Ala Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Ile Ser Phe
            340                 345                 350
His Ser Ala Trp Leu Thr Val Leu Pro Gly Ile Tyr Cys Ser Phe Ser
        355                 360                 365
Leu Gly Phe Phe Pro Phe Ser Trp Leu Thr Ala Ile Lys Leu Thr Gln
    370                 375                 380
Leu Leu Leu Ser Glu Met Ala Pro Phe Ile Leu Ala
385                 390                 395
```

<210> 185
<211> 1240
<212> DNA
<213> Homo Sapiens

<400> 185
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgata tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt taaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct aggcaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
gtaagtcaca tcagttcccc acttataaac tgtgaggtat   1240

<210> 186
<211> 413
<212> PRT

<213> Homo Sapiens

<400> 186

```
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1               5                  10                  15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35                  40                  45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Leu Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Val Ser His Ile Ser Ser Pro Leu Ile Asn Cys Glu Val
                405                 410
```

<210> 187
<211> 1405
<212> DNA
<213> Homo Sapiens

<400> 187
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaaa ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggtaagtgc tttct 1405

<210> 188
<211> 468
<212> PRT
<213> Homo Sapiens

<400> 188
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1   5   10   15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20   25   30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35   40   45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50   55   60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65   70   75   80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85   90   95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100   105   110
Lys Asn Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115   120   125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130   135   140

Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385 390 395 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
405 410 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
420 425 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
435 440 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
450 455 460
Val Ser Ala Phe
465

<210> 189
<211> 1557
<212> DNA
<213> Homo Sapiens

<400> 189
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacatttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacattaa catggctcta 360

gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgtc 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatgac 1500
tacacactgg ttatcactgg gaaggaggta agctgttccc acagggaatt tccatga 1557

<210> 190
<211> 518
<212> PRT
<213> Homo Sapiens

<400> 190
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu

225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Leu Asn Asp Val Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385 390 395 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
405 410 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
420 425 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
435 440 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
450 455 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465 470 475 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
485 490 495
Asn Gln Asn Asp Tyr Thr Leu Val Ile Thr Gly Lys Glu Val Ser Cys
500 505 510
Ser His Arg Glu Phe Pro
515

<210> 191
<211> 1789
<212> DNA
<213> Homo Sapiens

<400> 191
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660

gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagccc gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggtaggaatc tctaacagct ggcatacatg tttttgtttg 1740
gtgtttttt ttttttttg gtttggtttg gtttgttttt tgttttttt 1789

<210> 192
<211> 596
<212> PRT
<213> Homo Sapiens

<400> 192
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240

```
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Pro Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Gly Ile Ser Asn Ser Trp His Thr
                565                 570                 575
Cys Phe Cys Leu Val Phe Phe Phe Phe Phe Trp Phe Gly Leu Val Cys
            580                 585                 590
Phe Leu Phe Phe
        595
```

<210> 193
<211> 1936
<212> DNA
<213> Homo Sapiens

<400> 193
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120

tatcggcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggagag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgcctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agatcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcattgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacgcaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagagaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
gcagaaaatg tgctagattg gaggtgaaga ccctggagcc agagagccta ggcttagtcc 1260
tagccctgca ctgaagacac ttctgagaaa ttcatcaggc tgtgaagcgc gccgtgatga 1320
atatcgaaca gagtttacca cagctttgca gcgcgttgac ttattcatgg gtcaattcag 1380
cgaagtcctc ttaacatcta tatccacctt cattaaagga gacctcacca tagctaatct 1440
tgggacatca gagggtcgct tcatgcaggt tgtggtttct cgatcaggac catcaacccc 1500
tcatgtgaat tttctcctgg actcccatcc agtgtctcca gaagtgattg tggagcatac 1560
attaaaccaa aatggctaca cactggttat cactgggaag aagatcacga agatcccatt 1620
gaatggcttg ggctgcagac atttccagtc ctgcagtcaa tgcctctctg ccccaccctt 1680
tgttcagtgt ggctggtgcc acaacaaatg tgtgcgatcg gaggaatgcc tgagcgggac 1740
atggactcaa cagatctgtc tgcctgcaat ctacaaggta ggaatctcta acagctggca 1800
tacatgtttt tgtttggtgt ttttttttt tttttggttt ggtttggttt gttttttgtt 1860
tttttagata caaatcccac taatgaaaaa aatttaaaaa tcaatttact catttagctg 1920
tgagtcatca gctaaa 1936

<210> 194
<211> 408
<212> PRT
<213> Homo Sapiens

<400> 194
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1   5   10   15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20   25   30
Ser Glu Met Asn Val Asn Met Lys Tyr Arg Leu Pro Asn Phe Thr Ala
        35   40   45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50   55   60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65   70   75   80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85   90   95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100   105   110
Arg Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115   120   125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130   135   140

```
Ala Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Asp Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Leu Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Ala Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Ala Glu Asn Val Leu Asp Trp Arg
                405
```

<210> 195
<211> 1888
<212> DNA
<213> Homo Sapiens

<400> 195

```
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggctcactgc 480
atattctccc cacagataga agagcccagt cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
```

ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attctttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acgtaaggat cttaaaatgc tttgctgg 1888

<210> 196
<211> 621
<212> PRT
<213> Homo Sapiens

<400> 196
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Ala His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn

```
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr
    610                 615                 620
```

<210> 197
<211> 1995
<212> DNA
<213> Homo Sapiens

<400> 197
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60

aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
atggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggtaag gaagattcta 1980
tcctatcatg tttga 1995

<210> 198
<211> 664
<212> PRT
<213> Homo Sapiens

<400> 198
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1   5   10   15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20   25   30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35   40   45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50   55   60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65   70   75   80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85   90   95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100   105   110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115   120   125

```
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Met Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
```

```
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Val
                645                 650                 655
Arg Lys Ile Leu Ser Tyr His Val
            660
```

<210> 199
<211> 2170
<212> DNA
<213> Homo Sapiens

<400> 199
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cctggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat cctgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgttagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attctttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
cacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggatcc tgtaataaca 1980
agtatttcgc cgaaatacgg tcctatggct ggtggcactt tacttacttt aactggaaat 2040
tacctaaaca gtgggaattc tagacacatt tcaattggtg gaaaaacatg tactttaaaa 2100
aggtgttgta aatttatttt ttgttgcatc tgtcaatttg aattaatatc tgtaccttaa 2160

aaattaagca 2170

<210> 200
<211> 719
<212> PRT
<213> Homo Sapiens

<400> 200

```
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1               5                  10                  15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35                  40                  45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Val Phe Pro His Asn His Pro Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
```

```
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly His Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Arg Cys Cys Lys
    690                 695                 700
Phe Ile Phe Cys Cys Ile Cys Gln Phe Glu Leu Ile Ser Val Pro
705                 710                 715
```

<210> 201
<211> 2194
<212> DNA
<213> Homo Sapiens

<400> 201
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgc gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360

gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag gaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attctttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagaccc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acagtacagt acattctcct atgtgttact ttgttttgtt 1980
tttatctccc ctccaggatc ctgtaataac aagtatttcg ccgaaatacg gtcctatggc 2040
tggtggcact ttacttactt taactggaaa ttacctaaac agtgggaatt ctagacacat 2100
ttcaattggt ggaaaaacat gtactttaaa aaggtgttgt aaatttattt tttgttgcat 2160
ctgtcaattt gaattaatat ctgtacctta aaaa 2194

<210> 202
<211> 697
<212> PRT
<213> Homo Sapiens

<400> 202
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1   5   10   15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20   25   30
Ser Glu Met Asn Ala Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35   40   45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50   55   60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65   70   75   80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85   90   95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100   105   110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115   120   125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130   135   140

```
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Thr Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
```

```
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Leu
                645                 650                 655
Leu Cys Phe Val Phe Ile Ser Pro Pro Gly Ser Cys Asn Asn Lys Tyr
            660                 665                 670
Phe Ala Glu Ile Arg Ser Tyr Gly Trp Trp His Phe Thr Tyr Phe Asn
        675                 680                 685
Trp Lys Leu Pro Lys Gln Trp Glu Phe
    690                 695
```

<210> 203
<211> 2082
<212> DNA
<213> Homo Sapiens

<400> 203

```
aatgaaggcc cccgctgtgc ttgcacctgg catcctcgtg ctcctgttta ccttggtgca 60
gaggagcaat ggggagtgta aagaggcact agcaaagtcc gagatgaatg tgaatatgaa 120
gtatcagctt cccaacttca ccgcggaaac acccatccag aatgtcattc tacatgagca 180
tcacattttc cttggtgcca ctaactacat ttatgtttta aatgaggaag accttcagaa 240
ggttgctgag tacaagactg ggcctgtgct ggaacaccca gattgtttcc catgtcagga 300
ctgcagcagc aaagccaatt tatcaggagg tgtttggaaa gataacatca acatggctct 360
agttgtcgac acctactatg atgatcaact cattagctgt ggcagcgtca acagagggac 420
ctgccagcga catgtctttc cccacaatca tactgctgac atacagtcgg aggttcactg 480
catattctcc ccacagatag aagagcccag ccagtgtcct gactgtgtgg tgagcgccct 540
gggagccaaa gtcctttcat ctgtaaagga ccggttcatc aacttctttg taggcaatac 600
cataaattct tcttatttcc cagatcatcc attgcattcg atatcagtga gaaggctaaa 660
ggaaacgaaa gatggtttta tgtttttgac ggaccagtcc tacattgatg ttttacctga 720
gttcagagat tcttacccca ttaagtatgt ccatgccttt gaaagcaaca attttattta 780
cttcttgacg gtccaaaggg aaactctaga tgctcagact tttcacacaa gaataatcag 840
gttctgttcc ataaactctg gattgcattc ctacatggaa atgcctctgg agtgtattct 900
cacagaaaag agaaaaaaga gatccacaaa gaaggaagtg tttaatatac ttcaggctgc 960
gtatgtcagc aagcctgggg cccagcttgc tagacaaata ggagccagcc tgaatgatga 1020
cattcttttc ggggtgttcg cacaaagcaa gccagattct gccgaaccaa tggatcgatc 1080
tgccatgtgt gcattcccta tcaaatatgt caacgacttc ttcaacaaga tcgtcaacaa 1140
aaacaatgtg agatgtctcc agcattttta cggacccaat catgagcact gctttaatag 1200
gacacttctg agaaattcat caggctgtga agcgcgccgt gatgaatatc gaacagagtt 1260
taccacagct ttgcagcgcg ttgacttatt catgggtcaa ttcagcgaag tcctcttaac 1320
atctatatcc accttcatta aaggagacct caccatagct aatcttggga catcagaggg 1380
tcgcttcatg caggttgtgg tttctcgatc aggaccatca acccctcatg tgaattttct 1440
cctggactcc catccagtgt ctccagaagt gattgtggag catacattaa accaaaatgg 1500
ctacacactg gttatcactg ggaagaagtg tggctggcgc cacgacaaat gtgtgcgatc 1560
ggaggaatgc ctgagcggga catggactca acagatctgt ctgcctgcaa tctacaaggt 1620
tttcccaaat agtgcacccc ttgaaggagg gacaaggctg accatatgtg gctgggactt 1680
tggatttcgg aggaataata aatttgattt aaagaaaact agagttctcc ttggaaatga 1740
gagctgcacc ttgactttaa gtgagagcac gatgaataca ttgaaatgca cagttggtcc 1800
tgccatgaat aagcatttca atatgtccat aattatttca aatggccacg ggacaacaca 1860
atacagtaca ttctcctatg tggatcctgt aataacaagt atttcgccga aatacggtcc 1920
tatggctggt ggcactttac ttactttaac tggaaattac ctaaacagtg ggaattctag 1980
acacatttca attggtggaa aaacatgtac tctaaaaagg tgtggtaaat ttatttttg 2040
```

ttgcatctgt caatttgaat taatatctgt accttaaaaa tt 2082

<210> 204
<211> 691
<212> PRT
<213> Homo Sapiens

<400> 204
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380

```
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Cys Gly Trp
            500                 505                 510
Arg His Asp Lys Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp
        515                 520                 525
Thr Gln Gln Ile Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser
    530                 535                 540
Ala Pro Leu Glu Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe
545                 550                 555                 560
Gly Phe Arg Arg Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu
                565                 570                 575
Leu Gly Asn Glu Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn
            580                 585                 590
Thr Leu Lys Cys Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met
        595                 600                 605
Ser Ile Ile Ile Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe
    610                 615                 620
Ser Tyr Val Asp Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro
625                 630                 635                 640
Met Ala Gly Gly Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser
                645                 650                 655
Gly Asn Ser Arg His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys
            660                 665                 670
Arg Cys Gly Lys Phe Ile Phe Cys Cys Ile Cys Gln Phe Glu Leu Ile
        675                 680                 685
Ser Val Pro
    690
```

<210> 205
<211> 2294
<212> DNA
<213> Homo Sapiens

<400> 205
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480

atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc gcgaagatcc cattgaatgg cttgggttgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acagtacagt acattctcct atgtgctccc ctccaggatc 1980
ctgtaataac aagtatttcg ccgaaatacg gtcctatggc tggtggcact ttacttactt 2040
taactggaaa ttacctaaac agtgggaatt ctagacacat ttcaattggt ggaaaaacat 2100
gtactttaaa aagtgtgtca aacagtattc ttgaatgtta taccccagcc caaaccattt 2160
caactgagtt tgctgttaaa ttgaaaattg acttagccaa ccgagagaca agcatcttca 2220
gttaccgtga agatcccatt gtctatgaaa ttcatccaac caaatctttt attaggtaag 2280
tagaagcttc tgat 2294

<210> 206
<211> 661
<212> PRT
<213> Homo Sapiens

<400> 206
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1   5   10   15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20   25   30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35   40   45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50   55   60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65   70   75   80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85   90   95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100   105   110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115   120   125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130   135   140

```
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Ala Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
```

```
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Leu
                645                 650                 655
Pro Ser Arg Ile Leu
            660
```

<210> 207
<211> 3256
<212> DNA
<213> Homo Sapiens

<400> 207
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacgatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatggg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcgtgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg tttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgctacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acatcgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggatcc tgtaataaca 1980
agtatttcgc cgaaatacgg tcctatggct ggtggcactt tacttacttt aactggaaat 2040
tacctaaaca gtgggaattc tagacacatt tcaattggtg ggaaaacatg tactttaaaa 2100
agtgtgtcaa acagtattct tgaatgttat accccagccc aaaccatttc aactgagttt 2160
gctgttaaat tgaaaattga cttagccaac cgagagacaa gcatcttcag ttaccgtgaa 2220
gatcccattg tctatgtaat tcatccaacc aaatctttta ttaggtaagt agaagcttct 2280

gatgggtata agaaaacaat gaatacaagg atgattttgc tgtagaatag tcaagaggaa 2340
ttgcagtttt atctctggct ttgatgctgt tatgttgctt ttgaaggctt ctttccaatt 2400
caggagagaa aactatattc aggttctgag tgtagtttga cttatcaatg ctagttcatt 2460
ccaagaagta tcttatcctg ttctattaca tttaaacaga gtatagcaaa atagtttaat 2520
gtggcattgt agtatacatg cacttacatt atgtacatat caattctata ctaaccttag 2580
tgcccagaag tggaattacc ttttttcttc cattctctag atatgttttt gtcctgcctg 2640
ctttacacac agcttttctt tatgccagac tctctttgaa ttgatatctc attggaccca 2700
gttcaatctg ccttgttccc gttaattcta tcagtctagc aacaatagtt aagttcggtt 2760
ttctttgtat ttttttcaga ggtgaaatat ttattttgtg taattcggtg aataaaatac 2820
aaatgcattt cttaagctta tgaaatatgc attttaaaaa tattttcaag ttaaataagt 2880
tgtttccaaa gaacagttac ccatgaactt ccatttgatg ttgactgtgc ctctgacctg 2940
taatcagtgc aggtgattaa attgaatccc tctcttacag tacttggtgg aaagaacctc 3000
tcaacattgt cagttttcta ttttgctttg ccagtggtgg gagcacaata acaggtgttg 3060
ggaaaaacct gaattcagtt agtgtcccga gaatggtcat aaatgtgcat gaagcaggaa 3120
ggaactttac agtggtaagt cctttgagca atggttctac tcagagctct gcatctttgc 3180
ctctaaccat gtggctttca tggtacctga gacatctcag tttcgccttt aaggtttgct 3240
agttaatttc cttgca 3256

<210> 208
<211> 755
<212> PRT
<213> Homo Sapiens

<400> 208
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255

```
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asp Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Gly
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro Arg Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys Tyr Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Ser Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
```

```
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Val Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Arg
        755
```

<210> 209
<211> 2481
<212> DNA
<213> Homo Sapiens

<400> 209

```
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatacgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggatcc tgtaataaca 1980
agtatttcgc cgaaatacgg tcctatggct ggtggcactt tacttacttt aactggaaat 2040
tacctaaaca gtgggaattc tagacacatt tcaattggtg gaaaaacatg tactttaaaa 2100
agtgtgtcaa acagtattct tgaatgttat accccagccc aaaccatttc aactgagttt 2160
gctgttaaat tgaaaattga cttaaccaac cgagagacaa gcatcttcag ttaccgtgaa 2220
gatcccattg tctatgaaat tcatccaacc aaatctttta ttagtggtgg gagcacaata 2280
acaggtgttg ggaaaaacct gaattcagtt agtgtcccga gaatggtcat aaatgtgcat 2340
gaagcaggaa ggaactttac agtggtaagt cctttgagca atggttctac tcagagctct 2400
```

gcatctttgc ctctaaccat gtggctttca tggtacctga gacatctcag tttcgccttt 2460
aaggtttgct agttaatttc c 2481

<210> 210
<211> 823
<212> PRT
<213> Homo Sapiens

<400> 210
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Thr Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg

```
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Thr Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780
Asn Phe Thr Val Val Ser Pro Leu Ser Asn Gly Ser Thr Gln Ser Ser
785                 790                 795                 800
Ala Ser Leu Pro Leu Thr Met Trp Leu Ser Trp Tyr Leu Arg His Leu
                805                 810                 815
Ser Phe Ala Phe Lys Val Cys
```

820

<210> 211
<211> 2667
<212> DNA
<213> Homo Sapiens

<400> 211
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccgcaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcacca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgt tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagccc gaatgatgac 1020
attcttttcg gagtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttc 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaagaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcaacagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggatcc tgtaataaca 1980
agtatttcgc cgaaatacgg tcctatggct ggtggcactt tacttacttt aactggaaat 2040
tacctaaaca gtgggaattc tagacacatt tcaattggtg gaaaaacatg tactttaaaa 2100
agtgtgtcaa acagtattct tgaatgttat accccagccc aaaccatttc aactgagttt 2160
gctgttaaat tgaaaattga cttagccaac cgagagacaa gcatcttcag ttaccgtgaa 2220
gatcccattg tctatgaaat tcatccaacc aaatctttta ttagtggtgg gagcacaata 2280
acaggtgttg ggaaaaacct gaattcagtt agtgtcccga gaatggtcat aaatgtgcat 2340
gaagcgggaa ggaactttac agtggcatgt caacatcgct ctaattcaga gataatctgt 2400
tgtaccactc cttccctgca acagctgaat ctgcaactcc ccctgaaaac caaagccttt 2460
ttcatgttag atgggatcct ttccaaatac tttgatctca tttatgtaca taatcctgtg 2520
tttaagcctt ttgaaaagcc agtgatgatc tcaatgggca atgaaaatgt actggaaatt 2580
aaggtaagaa atgctttaaa cactgtctta aatcatcagc tcaaacttaa ttgacttcat 2640
agctatgtga atacaattgt tgtactt 2667

<210> 212

<211> 877
<212> PRT
<213> Homo Sapiens

<400> 212
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro Arg Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Thr Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Pro Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385 390 395 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr

```
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780
Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800
Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815
Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830
Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845
Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Val Arg Asn
```

```
    850                 855                 860
Ala Leu Asn Thr Val Leu Asn His Gln Leu Lys Leu Asn
865                 870                 875
```

<210> 213
<211> 2542
<212> DNA
<213> Homo Sapiens

<400> 213

```
atgaaggccc ccgctgtgct tgcacctggc atcctcgtgc tcctgtttac cttggtgcag 60
aggagcaatg gggagtgtaa agaggcacta gcaaagtccg agatgaatgt gaatatgaag 120
tatcagcttc ccaacttcac cgcggaaaca cccatccaga atgtcattct acatgagcat 180
cacattttcc ttggtgccac taactacatt tatgttttaa atgaggaaga ccttcagaag 240
gttgctgagt acaagactgg gcctgtgctg gaacacccag attgtttccc atgtcaggac 300
tgcagcagca aagccaattt atcaggaggt gtttggaaag ataacatcaa catggctcta 360
gttgtcgaca cctactatga tgatcaactc attagctgtg gcagcgtcaa cagagggacc 420
tgccagcgac atgtctttcc ccacaatcat actgctgaca tacagtcgga ggttcactgc 480
atattctccc cacagataga agagcccagc cagtgtcctg actgtgtggt gagcgccctg 540
ggagccaaag tcctttcatc tgtaaaggac cggttcatca acttctttgt aggcaatacc 600
ataaattctt cttatttccc agatcatcca ttgcattcga tatcagtgag aaggctaaag 660
gaaacgaaag atggttttat gtttttgacg gaccagtcct acattgatgc tttacctgag 720
ttcagagatt cttaccccat taagtatgtc catgcctttg aaagcaacaa ttttatttac 780
ttcttgacgg tccaaaggga aactctagat gctcagactt ttcacacaag aataatcagg 840
ttctgttcca taaactctgg attgcattcc tacatggaaa tgcctctgga gtgtattctc 900
acagaaaaga gaaaaaagag atccacaaag aaggaagtgt ttaatatact tcaggctgcg 960
tatgtcagca agcctggggc ccagcttgct agacaaatag gagccagcct gaatgatgac 1020
attcttttcg gggtgttcgc acaaagcaag ccagattctg ccgaaccaat ggatcgatct 1080
gccatgtgtg cattccctat caaatatgtc aacgacttct tcaacaagat cgtcaacaaa 1140
aacaatgtga gatgtctcca gcatttttac ggacccaatc atgagcactg ctttaatagg 1200
acacttctga gaaattcatc aggctgtgaa gcgcgccgtg atgaatatcg aacagagttt 1260
accacagctt tgcagcgcgt tgacttattc atgggtcaat tcagcgaagt cctcttaaca 1320
tctatatcca ccttcattaa aggagacctc accatagcta atcttgggac atcagagggt 1380
cgcttcatgc aggttgtggt ttctcgatca ggaccatcaa cccctcatgt gaattttctc 1440
ctggactccc atccagtgtc tccagaagtg attgtggagc atacattaaa ccaaaatggc 1500
tacacactgg ttatcactgg gaggaagatc acgaagatcc cattgaatgg cttgggctgc 1560
agacatttcc agtcctgcag tcaatgcctc tctgccccac cctttgttca gtgtggctgg 1620
tgccacgaca aatgtgtgcg atcggaggaa tgcctgagcg ggacatggac tcagcagatc 1680
tgtctgcctg caatctacaa ggttttccca aatagtgcac cccttgaagg agggacaagg 1740
ctgaccatat gtggctggga ctttggattt cggaggaata ataaatttga tttaaagaaa 1800
actagagttc tccttggaaa tgagagctgc accttgactt taagtgagag cacgatgaat 1860
acattgaaat gcacagttgg tcctgccatg aataagcatt tcaatatgtc cataattatt 1920
tcaaatggcc acgggacaac acaatacagt acattctcct atgtggatcc tgtaataaca 1980
agtatttcgc cgaaatacgg tcctatggct ggtggcactt tacttacttt aactggaaat 2040
tacctaaaca gtgggaattc tagacacatt tcaattggtg gaaaaacgtg tactttaaaa 2100
agtgtgtcaa acagtattct tgaatgttat accccagccc aaaccatttc aactgagtct 2160
gctgttaaat tgaaaattga cttagccaac cgagagacaa gcatcttcag ttaccgtgaa 2220
gatcccattg tctatgaaat tcatccaacc aaatctttta ttaggcatgt caacatcgct 2280
ctaattcaga gataatctgt tgtaccactc cttccctgca acagctgaat ctgcaactcc 2340
ccctgaaaac caaagccttt ttcatgttag atgggatcct ttccaaatac tttgatctca 2400
tttatgtaca taatcctgtg tctaagcctt ttggaaagcc agtgatgatc tcaatgggca 2460
atgaaaatgt actggaaatt aagataagaa atgctttaaa cactgtctta aatcatcagc 2520
tcaaacttaa ttgacttcat ag                                          2542
```

<210> 214

<211> 764
<212> PRT
<213> Homo Sapiens

<400> 214
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
35 40 45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Ala Leu Pro Glu
225 230 235 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
245 250 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
260 265 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
275 280 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
290 295 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305 310 315 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
325 330 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
340 345 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
355 360 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
370 375 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385 390 395 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr

```
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Arg Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Ser
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Arg His Val Asn Ile Ala Leu Ile Gln Arg
        755                 760
```

<210> 215
<211> 3113
<212> DNA
<213> Homo Sapiens

<400> 215
ggtcccagct cgcctcgatg gagctcctcc cgccgctgcc tcagtccttc ctgttgctgc 60
tgctgttgcc tgccaagccc gcggcgggcg aggactggca gtgcccgcgc acccccctacg 120
cggcctctcg cgactttgac gtgaagtacg tggtgcccag cttctccgcc ggaggcctgg 180

tacaggccat ggtgacctac gagggcgaca gaaatgagag tgctgtgttt gtagccatac 240
gcaatcgcct gcatgtgctt gggcctgacc tgaagtctgt ccagagcctg gccacgggcc 300
ctgctggaga ccctggctgc cagacgtgtg cagcctgtgg cccaggaccc cacggccctc 360
ccggtgacac agacacaaag gtgctggtgc tggatcccgc gctgcctgcg ctggtcagtt 420
gtggctccag cctgcagggc cgctgcttcc tgcatgacct agagccccaa gggacagccg 480
tgcatctggc agcgccagcc tgcctcttct cagcccacca taaccggccc gatgactgcc 540
ccgactgtgt ggccagccca ttgggcaccc gtgtaactgt ggttgagcaa ggccaggcct 600
cctatttcta cgtggcatcc tcactggacg cagccgtggc tgccagcttc agcccacgct 660
cagtgtctat caggcgtctc aaggctgacg cctcgggatt cgcaccgggc tttgtggcgt 720
tgtcagtgct gcccaagcat cttgtctcct acagtattga atacgtgcac agcttccaca 780
cgggagcctt cgtatacttc ctgactgtac agccggccag cgtgacagat gatcctagtg 840
ccctgcacac acgcctggca cggcttagcg ccactgagcc agagttgggt gactatcggg 900
agctggtcct cgactgcaga tttgctccaa aacgcaggcg ccgggggccc ccagaaggcg 960
gacagcccta ccctgtgctg cgggtggccc actccgctcc agtgggtgcc caacttgcca 1020
ctgagctgag catcgccgag ggccaggaag tactatttgg ggtctttgtg actggcaagg 1080
atggtggtcc tggcgtgggc cccaactctg tcgtctgtgc cttccccatt gacctgctgg 1140
acacactaat tgatgagggt gtggagcgct gttgtgaatc cccagtccat ccaggcctcc 1200
ggcgaggcct cgacttcttc cagtcgccca gtttttgccc caacccggtt ttccaggtac 1260
ctatccaagg ccctggctgc cgccacttcc tgacctgtgg gcgttgccta agggcatggc 1320
atttcatggg ctgtggctgg tgtgggaaca tgtgcggcca gcagaaggag tgtcctggct 1380
cctggcaaca ggaccactgc ccacctaagc ttactgagtt ccacccccac agtggacctc 1440
taaggggcag tacaaggctg accctgtgtg gctccaactt ctaccttcac ccttctggtc 1500
tggtgcctga gggaacccat caggtcactg tgggccaaag tccctgccgg ccactgccca 1560
aggacagctc aaaactcagg tacaatctgg tccctccctt ccctttccct gaaggggggaa 1620
accaagcagc cccttcccca tgagaccctg ttctctgctt atcagaggca agggggggatg 1680
ggggaagctg cagtggttct gactgctttt tgagagtcaa aaaggtctct gtccctttt 1740
gagctttcat gtgcccttcc tgtctgttca ctcatggacc agccaaggtt aatctctgcc 1800
ccaccagaac cttccttcca tggagggagg catgggtgga gaaatgccat tctctggctc 1860
agaggagccc tgtggcttgt ggcaggcatg catctaggcc tgtgtaattc ctggctgacc 1920
tcaggggttc ccctggtgcc ccagaccagt gccccggaaa gactttgtag aggagtttga 1980
gtgtgaactg gagcccttgg gcacccaggc agtggggcct accaacgtca gcctcaccgt 2040
gactaacatg ccaccgggca agcacttccg ggtagacggc acctccgtgc tgagaggctt 2100
ctctttcatg gagccagtgc tgatagcagt gcaacccctc tttggcccac gggcaggagg 2160
cacctgtctc actcttgaag gccagagtct gtctgtaggc accagccggg ctgtgctggt 2220
caatgggact gagtgtctgc tagcacgggt cagtgagggg cagcttttat gtgccacacc 2280
ccctggggcc acggtggcca gtgtcccccct tagcctgcag gtgggggggtg cccaggtacc 2340
tggttcctgg accttccagt acagagaaga ccctgtcgtg ctaagcatca gccccaactg 2400
tggctacatc aactcccaca tcaccatctg tggccagcat ctaacttcag catggcactt 2460
agtgctgtca ttccatgacg ggcttagggc agtggaaagc aggtgtgaga ggcagcttcc 2520
agagcagcag ctgtgccgcc ttcctgaata tgtggtccga gacccccagg gatgggtggc 2580
agggaatctg agtgcccgag gggatggagc tgctggcttt acactgcctg gctttcgctt 2640
cctaccccca ccccatccac ccagtgccaa cctagttcca ctgaagcctg aggagcatgc 2700
cattaagttt gaggtaagtg taagggatag gggcagggac agttggggat ctgaaagtag 2760
gggccagcct actggctggt cctcatgacc ctctctgcag tatattgggc tgggcgctgt 2820
ggctgactgt gtgggtatca acgtgaccgt gggtggtgag agctgccagc acgagttccg 2880
gggggacatg gttgtctgcc ccctgccccc atccctgcag cttggccagg atggtgcccc 2940
attgcaggtc tgcgtagatg gtgaatgtca tatcctgggt agagtggtgc ggccagggcc 3000
agatggggtc ccacagagca cgctccttgg tatcctgctg cctttgctgc tgcttgtggc 3060
tgcactggcg actgcactgg tcttcagcta ctggtggcgg aggaagcagc tag 3113

<210> 216
<211> 541
<212> PRT
<213> Homo Sapiens

<400> 216

```
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1               5                  10                  15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20                  25                  30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35                  40                  45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50                  55                  60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65                  70                  75                  80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85                  90                  95
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100                 105                 110
Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115                 120                 125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145                 150                 155                 160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205
Ala Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Arg Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Val Phe Gln Val Pro Ile
                405                 410                 415
Gln Gly Pro Gly Cys Arg His Phe Leu Thr Cys Gly Arg Cys Leu Arg
            420                 425                 430
Ala Trp His Phe Met Gly Cys Gly Trp Cys Gly Asn Met Cys Gly Gln
        435                 440                 445
```

```
Gln Lys Glu Cys Pro Gly Ser Trp Gln Gln Asp His Cys Pro Pro Lys
    450                 455                 460
Leu Thr Glu Phe His Pro His Ser Gly Pro Leu Arg Gly Ser Thr Arg
465                 470                 475                 480
Leu Thr Leu Cys Gly Ser Asn Phe Tyr Leu His Pro Ser Gly Leu Val
                485                 490                 495
Pro Glu Gly Thr His Gln Val Thr Val Gly Gln Ser Pro Cys Arg Pro
            500                 505                 510
Leu Pro Lys Asp Ser Ser Lys Leu Arg Tyr Asn Leu Val Pro Pro Leu
        515                 520                 525
Pro Phe Pro Glu Gly Gly Asn Gln Ala Ala Pro Ser Pro
    530                 535                 540
```

<210> 217
<211> 3069
<212> DNA
<213> Homo Sapiens

<400> 217

```
ggtcccagct cgcctcgatg gagctcctcc cgccgctgcc tcagtccttc ctgttgctgc 60
tgctgttgcc tgccaagccc gcggcgggcg aggactggca gtgcccgcgc acccccctacg 120
cggcctctcg cgactttgac gtgaagtacg tggtgcccag cttctccgcc ggaggcctgg 180
tacaggccat ggtgacctac gagggcgaca gaaatgagag tgctgtgttt gtagccatac 240
gcaatcgcct gcatgtgctt gggcctgacc tgaagtctgt ccagagcctg gccacgggcc 300
ctgctggaga ccctggctgc cagacgtgtg cagcctgtgg cccaggaccc cacggccctc 360
ccggtgacac agacacaaag gtgctggtgc tggatcccgc gctgcctgcg ctggtcagtt 420
gtggctccag cctgcagggc cgctgcttcc tgcatgacct agagccccaa gggacagccg 480
tgcatctggc agcgccagcc tgcctcttct cagcccacca taaccggccc gatgactgcc 540
ccgactgtgt ggccagccca ttgggcaccc gtgtaactgt ggttgagcaa ggccaggcct 600
cctatttcta cgtggcatcc tcactggacg cagccgtggc tgccagcttc agcccacgct 660
cagtgtctat caggcgtctc aaggctgacg cctcgggatt cgcaccgggc tttgtggcgt 720
tgtcagtgct gcccaagcat cttgtctcct acagtattga atacgtgcac agcttccaca 780
cgggagcctt cgtatacttc ctgactgtac agccggccag cgtgacagat gatcctagtg 840
ccctgcacac acgcctggca cggcttagcg ccactgagcc agagttgggt gactatcggg 900
agctggtcct cgactgcaga tttgctccaa aacgcaggcg ccgggggccc ccagaaggcg 960
gacagcccta ccctgtgctg cgggtggccc actccgctcc agtgggtgcc caacttgcca 1020
ctgagctgag catcgccgag ggccaggaag tactatttgg ggtctttgtg actggcaagg 1080
atggtggtcc tggcgtgggc cccaactctg tcgtctgtgc cttccccatt gacctgctgg 1140
acacactaat tgatgagggt gtggagcgct gttgtgaatc cccagtccat ccaggcctcc 1200
ggcgaggcct cgacttcttc cagtcgccca gtttttgccc caacccgcct ggcctggaag 1260
ccctcagccc caacaccagc tgccgccact tccctctgct ggtcagtagc agcttctcac 1320
gtgtggacct attcaatggg ctgttgggac cagtacaggt cactgcattg tatgtgacac 1380
gccttgacaa cgtcacagtg gcacacatgg gcacaatgga tgggcgtatc ctgcaggtgg 1440
agctggtcag gtcactaaac tacttgctgt atgtgtccaa cttctcactg ggtgacagtg 1500
ggcagcccgt gcagcgggat gtcagtcgtc ttggggacca cctactcttt gcctctgggg 1560
accaggtttt ccaggtacct atccaaggcc ctggctgccg ccacttcctg acctgtgggc 1620
gttgcctaag ggcatggcat ttcatgggct gtggctggtg tgggaacatg tgcggccagc 1680
agaaggagtg tcctggctcc tggcaacagg accactgccc acctaagctt actgagttcc 1740
acccccacag tggacctcta aggggcagta caaggctgac cctgtgtggc tccaacttct 1800
accttcaccc ttctggtctg gtgcctgagg gaacccatca ggtcactgtg ggccaaagtc 1860
cctgccggcc actgcccaag gacagctcaa aactcagacc agtgccccgg aaagactttg 1920
tagaggagtt tgagtgtgaa ctggagccct tgggcaccca ggcagtgggg cctaccaacg 1980
tcagcctcac cgtgactaac atgccaccgg gcaagcactt ccgggtagac ggcacctccg 2040
tgctgagagg cttctctttc atggagccag tgctgatagc agtgcaaccc ctctttggcc 2100
cacgggcagg aggcacctgt ctcactcttg aaggccagag tctgtctgta ggcaccagcc 2160
```

gggctgtgct ggtcaatggg actgagtgtc tgctagcacg ggtcagtgag gggcagcttt 2220
tatgtgccac acccccctggg gccacggtgg ccagtgtccc ccttagcctg caggtggggg 2280
gtgcccaggt acctggttcc tggaccttcc agtacagaga agaccctgtc gtgctaagca 2340
tcagccccaa ctgtggctac atcaactccc acatcaccat ctgtggccag catctaactt 2400
cagcatggca cttagtgctg tcattccatg acgggcttag ggcagtggaa agcaggcagt 2460
gtgagaggca gcttccagag cagcagctgt gccgccttcc tgaatatgtg gtccgagacc 2520
cccagggatg ggtggcaggg aatctgagtg cccgagggga tggagctgct ggctttacac 2580
tgcctggctt tcgcttccta cccccacccc atccacccag tgccaaccta gttccactga 2640
agcctgagga gcatgccatt aagtttgagg taagtgtaag ggataggggc agggacagtt 2700
ggggatctga aagtaggggc cagcctactg gctggtcctc atgaccctct ctgcagtata 2760
ttgggctggg cgctgtggct gactgtgtgg gtatcaacgt gaccgtgggt ggtgagagct 2820
gccagcacga gttccggggg gacatggttg tctgcccccc gcccccatcc ctgcagcttg 2880
gccaggatgg tgccccattg caggtctgcg tagatggtga atgtcatatc ctgggtagag 2940
tggtgcggcc agggccagat ggggtcccac agagcacgct ccttggtatc ctgctgcctt 3000
tgctgctgct tgtggctgca ctggcgactg cactggtctt cagctactgg tggcggagga 3060
agcagctag 3069

<210> 218
<211> 908
<212> PRT
<213> Homo Sapiens

<400> 218
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1   5   10   15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20   25   30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35   40   45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50   55   60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65   70   75   80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85   90   95
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100   105   110
Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115   120   125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130   135   140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145   150   155   160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165   170   175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180   185   190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195   200   205
Ala Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210   215   220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225   230   235   240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245   250   255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp

```
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Arg Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415
Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
            420                 425                 430
Phe Ser Arg Val Asp Leu Phe Asn Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445
Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460
Gly Thr Met Asp Gly Arg Ile Leu Gln Val Glu Leu Val Arg Ser Leu
465                 470                 475                 480
Asn Tyr Leu Leu Tyr Val Ser Asn Phe Ser Leu Gly Asp Ser Gly Gln
                485                 490                 495
Pro Val Gln Arg Asp Val Ser Arg Leu Gly Asp His Leu Leu Phe Ala
            500                 505                 510
Ser Gly Asp Gln Val Phe Gln Val Pro Ile Gln Gly Pro Gly Cys Arg
        515                 520                 525
His Phe Leu Thr Cys Gly Arg Cys Leu Arg Ala Trp His Phe Met Gly
    530                 535                 540
Cys Gly Trp Cys Gly Asn Met Cys Gly Gln Gln Lys Glu Cys Pro Gly
545                 550                 555                 560
Ser Trp Gln Gln Asp His Cys Pro Pro Lys Leu Thr Glu Phe His Pro
                565                 570                 575
His Ser Gly Pro Leu Arg Gly Ser Thr Arg Leu Thr Leu Cys Gly Ser
            580                 585                 590
Asn Phe Tyr Leu His Pro Ser Gly Leu Val Pro Glu Gly Thr His Gln
        595                 600                 605
Val Thr Val Gly Gln Ser Pro Cys Arg Pro Leu Pro Lys Asp Ser Ser
    610                 615                 620
Lys Leu Arg Pro Val Pro Arg Lys Asp Phe Val Glu Glu Phe Glu Cys
625                 630                 635                 640
Glu Leu Glu Pro Leu Gly Thr Gln Ala Val Gly Pro Thr Asn Val Ser
                645                 650                 655
Leu Thr Val Thr Asn Met Pro Pro Gly Lys His Phe Arg Val Asp Gly
            660                 665                 670
Thr Ser Val Leu Arg Gly Phe Ser Phe Met Glu Pro Val Leu Ile Ala
        675                 680                 685
Val Gln Pro Leu Phe Gly Pro Arg Ala Gly Gly Thr Cys Leu Thr Leu
    690                 695                 700
Glu Gly Gln Ser Leu Ser Val Gly Thr Ser Arg Ala Val Leu Val Asn
```

```
705                 710                 715                 720
Gly Thr Glu Cys Leu Leu Ala Arg Val Ser Glu Gly Gln Leu Leu Cys
                725                 730                 735
Ala Thr Pro Pro Gly Ala Thr Val Ala Ser Val Pro Leu Ser Leu Gln
            740                 745                 750
Val Gly Gly Ala Gln Val Pro Gly Ser Trp Thr Phe Gln Tyr Arg Glu
        755                 760                 765
Asp Pro Val Val Leu Ser Ile Ser Pro Asn Cys Gly Tyr Ile Asn Ser
    770                 775                 780
His Ile Thr Ile Cys Gly Gln His Leu Thr Ser Ala Trp His Leu Val
785                 790                 795                 800
Leu Ser Phe His Asp Gly Leu Arg Ala Val Glu Ser Arg Gln Cys Glu
                805                 810                 815
Arg Gln Leu Pro Glu Gln Gln Leu Cys Arg Leu Pro Glu Tyr Val Val
            820                 825                 830
Arg Asp Pro Gln Gly Trp Val Ala Gly Asn Leu Ser Ala Arg Gly Asp
        835                 840                 845
Gly Ala Ala Gly Phe Thr Leu Pro Gly Phe Arg Phe Leu Pro Pro Pro
    850                 855                 860
His Pro Pro Ser Ala Asn Leu Val Pro Leu Lys Pro Glu Glu His Ala
865                 870                 875                 880
Ile Lys Phe Glu Val Ser Val Arg Asp Arg Gly Arg Asp Ser Trp Gly
                885                 890                 895
Ser Glu Ser Arg Gly Gln Pro Thr Gly Trp Ser Ser
            900                 905
```

<210> 219
<211> 3500
<212> DNA
<213> Homo Sapiens

<400> 219

```
ggtcccagct cgcctcgatg gagctcctcc cgccgctgcc tcagtccttc ctgttgctgc 60
tgctgttgcc tgccaagccc gcggcgggcg aggactggca gtgcccgcgc acccctacg 120
cggcctctcg cgactttgac gtgaagtacg tggtgcccag cttctccgcc ggaggcctgg 180
tacaggccat ggtgacctac gagggcgaca gaaatgagag tgctgtgttt gtagccatac 240
gcaatcgcct gcatgtgctt gggcctgacc tgaagtctgt ccagagcctg gccacgggcc 300
ctgctggaga ccctggctgc cagacgtgtg cagcctgtgg cccaggaccc cacggccctc 360
ccggtgacac agacacaaag gtgctggtgc tggatcccgc gctgcctgcg ctggtcagtt 420
gtggctccag cctgcagggc cgctgcttcc tgcatgacct agagccccaa gggacagccg 480
tgcatctggc agcgccagcc tgcctcttct cagcccacca taaccggccc gatgactgcc 540
ccgactgtgt ggccagccca ttgggcaccc gtgtaactgt ggttgagcaa ggccaggcct 600
cctatttcta cgtggcatcc tcactggacg cagccgtggc tgccagcttc agcccacgct 660
cagtgtctat caggcgtctc aaggctgacg cctcgggatt cgcaccgggc tttgtggcgt 720
tgtcagtgct gcccaagcat cttgtctcct acagtattga atacgtgcac agcttccaca 780
cgggagcctt cgtatacttc ctgactgtac agccggccag cgtgacagat gatcctagtg 840
ccctgcacac acgcctggca cggcttagcg ccactgagcc agagttgggt gactatcggg 900
agctggtcct cgactgcaga tttgctccaa aacgcaggcg ccgggggccc ccagaaggcg 960
gacagcccta ccctgtgctg cgggtggccc actccgctcc agtgggtgcc caacttgcca 1020
ctgagctgag catcgccgag ggccaggaag tactatttgg ggtctttgtg actggcaagg 1080
atggtggtcc tggcgtgggc cccaactctg tcgtctgtgc cttccccatt gacctgctgg 1140
acacactaat tgatgagggt gtggagcgct gttgtgaatc cccagtccat ccaggcctcc 1200
ggcgaggcct cgacttcttc cagtcgccca gtttttgccc caacccgcct ggcctggaag 1260
ccctcagccc caacaccagc tgccgccact tccctctgct ggtcagtagc agcttctcac 1320
gtgtggacct attcaatggg ctgttgggac cagtacaggt cactgcattg tatgtgacac 1380
```

gccttgacaa cgtcacagtg gcacacatgg gcacaatgga tgggcgtatc ctgcaggtgg 1440
agctggtcag gtcactaaac tacttgctgt atgtgtccaa cttctcactg ggtgacagtg 1500
ggcagcccgt gcagcgggat gtcagtcgtc ttggggacca cctactcttt gcctctgggg 1560
accaggtttt ccaggtacct atccaaggcc ctggctgccg ccacttcctg acctgtgggc 1620
gttgcctaag ggcatggcat ttcatgggct gtggctggtg tgggaacatg tgcggccagc 1680
agaaggagtg tcctggctcc tggcaacagg accactgccc acctaagctt actgagttcc 1740
acccccacag tggacctcta aggggcagta caaggctgac cctgtgtggc tccaacttct 1800
accttcaccc ttctggtctg gtgcctgagg gaacccatca ggtcactgtg ggccaaagtc 1860
cctgccggcc actgcccaag gacagctcaa aactcaggta caatctggtc cctcccctcc 1920
ctttccctga agggggaaac caagcagccc cttccccatg agaccctgtt ctctgcttat 1980
cagaggcaag gggggatggg ggaagctgca gtggttctga ctgctttttg agagtcaaaa 2040
aggtctctgt ccctttttga gctttcatgt gcccttcctg tctgttcact catggaccag 2100
ccaaggttaa tctctgcccc accagaacct tccttccatg gagggaggca tgggtggaga 2160
aatgccattc tctggctcag aggagccctg tggcttgtgg caggcatgca tctaggcctg 2220
tgtaattcct ggctgacctc aggggttccc ctggtgcccc agaccagtgc cccggaaaga 2280
ctttgtagag gagtttgagt gtgaactgga gcccttgggc acccaggcag tggggcctac 2340
caacgtcagc ctcaccgtga ctaacatgcc accgggcaag cacttccggg tagacggcac 2400
ctccgtgctg agaggcttct ctttcatgga gccagtgctg atagcagtgc aacccctctt 2460
tggcccacgg gcaggaggca cctgtctcac tcttgaaggc cagagtctgt ctgtaggcac 2520
cagccgggct gtgctggtca atgggactga gtgtctgcta gcacgggtca gtgaggggca 2580
gcttttatgt gccacacccc ctggggccac ggtggccagt gtccccctta gcctgcaggt 2640
gggggggtgcc caggtacctg gttcctggac cttccagtac agagaagacc ctgtcgtgct 2700
aagcatcagc cccaactgtg gctacatcaa ctcccacatc accatctgtg gccagcatct 2760
aacttcagca tggcacttag tgctgtcatt ccatgacggg cttagggcag tggaaagcag 2820
gtgtgagagg cagcttccag agcagcagct gtgccgcctt cctgaatatg tggtccgaga 2880
cccccaggga tgggtggcag ggaatctgag tgcccgaggg gatggagctg ctggctttac 2940
actgcctggc tttcgcttcc tacccccacc ccatccaccc agtgccaacc tagttccact 3000
gaagcctgag gagcatgcca ttaagtttga ggtaagtgta agggataggg gcagggacag 3060
ttggggatct gaaagtaggg gccagcctac tggctggtcc tcatgaccct ctctgcagta 3120
tattgggctg ggcgctgtgg ctgactgtgt gggtatcaac gtgaccgtgg gtggtgagag 3180
ctgccagcac gagttccggg gggacatggt tgtctgcccc ctgcccccat ccctgcagct 3240
tggccaggat ggtgccccat tgcaggtagg cagcccagct ggacctccct gggaaacacg 3300
ggcagagggc ctacaggctg ggcctgagtt gccacctgcc cccaggtctg cgtagatggt 3360
gaatgtcata tcctgggtag agtggtgcgg ccagggccag atggggtccc acagagcacg 3420
ctccttggta tcctgctgcc tttgctgctg cttgtggctg cactggcgac tgcactggtc 3480
ttcagctact ggtggcggag 3500

<210> 220
<211> 647
<212> PRT
<213> Homo Sapiens

<400> 220
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1   5   10   15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20   25   30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35   40   45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50   55   60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65   70   75   80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85   90   95
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His

```
                100                 105                 110
Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
            115                 120                 125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145                 150                 155                 160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205
Ala Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Arg Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415
Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
            420                 425                 430
Phe Ser Arg Val Asp Leu Phe Asn Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445
Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460
Gly Thr Met Asp Gly Arg Ile Leu Gln Val Glu Leu Val Arg Ser Leu
465                 470                 475                 480
Asn Tyr Leu Leu Tyr Val Ser Asn Phe Ser Leu Gly Asp Ser Gly Gln
                485                 490                 495
Pro Val Gln Arg Asp Val Ser Arg Leu Gly Asp His Leu Leu Phe Ala
            500                 505                 510
Ser Gly Asp Gln Val Phe Gln Val Pro Ile Gln Gly Pro Gly Cys Arg
        515                 520                 525
His Phe Leu Thr Cys Gly Arg Cys Leu Arg Ala Trp His Phe Met Gly
    530                 535                 540
Cys Gly Trp Cys Gly Asn Met Cys Gly Gln Gln Lys Glu Cys Pro Gly
```

545 550 555 560
Ser Trp Gln Gln Asp His Cys Pro Pro Lys Leu Thr Glu Phe His Pro
565 570 575
His Ser Gly Pro Leu Arg Gly Ser Thr Arg Leu Thr Leu Cys Gly Ser
580 585 590
Asn Phe Tyr Leu His Pro Ser Gly Leu Val Pro Glu Gly Thr His Gln
595 600 605
Val Thr Val Gly Gln Ser Pro Cys Arg Pro Leu Pro Lys Asp Ser Ser
610 615 620
Lys Leu Arg Tyr Asn Leu Val Pro Pro Leu Pro Phe Pro Glu Gly Gly
625 630 635 640
Asn Gln Ala Ala Pro Ser Pro
645

<210> 221
<211> 2273
<212> DNA
<213> Homo Sapiens

<400> 221
ctctggagta tggtctggcg ggtgccccct ttcttgctcc ccatcctctt cttggcttct 60
catgtgggcg cggcggtgga cctgacgctg ctggccaacc tgcggctcac ggacccccag 120
cgcttcttcc tgacttgcgt gtctggggag gccggggcgg ggaggggctc ggacgcctgg 180
ggcccgcccc tgctgctgga gaaggacgac cgtatcgtgc gcaccccgcc cgggccaccc 240
ctgcgcctgg cgcgcaacgg ttcgcaccag gtcacgcttc gcggcttctc caagccctcg 300
gacctcgtgg gcgtcttctc ctgcgtgggc ggtgctgggg cgcggcgcac gcgcgtcatc 360
tacgtgcaca acagccctgg agcccacctg cttccagaca aggtcacaca cactgtgaac 420
aaaggtgaca ccgctgtact ttctgcacgt gtgcacaagg agaagcagac agacgtgatc 480
tggaagagca acggatccta cttctacacc ctggactggc atgaagccca ggatgggcgg 540
ttcctgctgc agctcccaaa tgtgcagcca ccatcgagcg gcatctacag tgccacttac 600
ctggaagcca gccccctggg cagcgccttc tttcggctca tcgtgcgggg ttgtggggct 660
gggcgctggg ggccaggctg taccaaggag tgcccaggtt gcctacatgg aggtgtctgc 720
cacgaccatg acggcgaatg tgtatgcccc cctggcttca ctggcacccg ctgtgaacag 780
gcctgcagag agggccgttt tgggcagagc tgccaggagc agtgcccagg catatcaggc 840
tgccggggcc tcaccttctg cctcccagac ccctatggct gctcttgtgg atctggctgg 900
agaggaagcc agtgccaaga agcttgtgcc cctggtcatt ttggggctga ttgccgactc 960
cagtgccagt gtcagaatgg tggcacttgt gaccggttca gtggttgtgt ctgcccctct 1020
gggtggcatg gagtgcactg tgagaagtca gaccggatcc cccagatcct caacatggcc 1080
tcagaactgg agttcaactt agagacgatg ccccggatca actgtgcagc tgcagggaac 1140
cccttccccg tgcggggcag catagagcta cgcaagccag acggcactgt gctcctgtcc 1200
accaaggcca ttgtggagcc agagaagacc acagctgagt tcgaggtgcc ccgcttggtt 1260
cttgcggaca gtgggttctg ggagtgccgt gtgtccacat ctggcggcca agacagccgg 1320
cgcttcaagg tcaatgtgaa agtgcccccc gtgcccctgg ctgcacctcg gctcctgacc 1380
aagcagagcc gccagcttgt ggtctccccg ctggtctcgt tctctgggga tggacccatc 1440
tccactgtcc gcctgcacta ccggccccag gacagtacca tggactggtc gaccattgtg 1500
gtggacccca gtgagaacgt gacgttaatg aacctgaggc caaagacagg atacagtgtt 1560
cgtgtgcagc tgagccggcc aggggaagga ggagaggggg cctgggggcc tcccaccctc 1620
atgaccacag actgtcctga gcctttgttg cagccgtggt tggagggctg gcatgtggaa 1680
ggcactgacc ggctgcgagt gagctggtcc ttgcccttgg tgcccgggcc actggtgggc 1740
gacggtttcc tgctgcgcct gtgggacggg acacgggggc aggagcggcg ggagaacgtc 1800
tcatcccccc aggcccgcac tgccctcctg acgggactca cgcctggcac ccactaccag 1860
ctggatgtgc agctctacca ctgcaccctc ctgggcccgg cctcgccccc tgcacacgtg 1920
cttctgcccc ccagtgggcc tccagccccc cgacacctcc acgcccaggc cctctcagac 1980
tccgagatcc agctgacatg gaagcacccg gaggctctgc ctgggccaat atccaagtac 2040
gttgtggagg tgcaggtggc tgggggtgca ggagacccac tgtggataga cgtggacagg 2100

cctgaggaga caagcaccat catccgtggc ctcaacgcca gcacgcgcta cctcttccgc 2160
atgcgggcca gcattcaggg gctcggggac tggagcaaca cagtagaaga gtccaccctg 2220
ggcaacggtg agagggcagg gcccacagga ccccccgggc tctgagcggg gag 2273

<210> 222
<211> 751
<212> PRT
<213> Homo Sapiens

<400> 222

Met	Val	Trp	Arg	Val	Pro	Pro	Phe	Leu	Leu	Pro	Ile	Leu	Phe	Leu	Ala
1				5					10					15	
Ser	His	Val	Gly	Ala	Ala	Val	Asp	Leu	Thr	Leu	Leu	Ala	Asn	Leu	Arg
			20					25					30		
Leu	Thr	Asp	Pro	Gln	Arg	Phe	Phe	Leu	Thr	Cys	Val	Ser	Gly	Glu	Ala
		35					40					45			
Gly	Ala	Gly	Arg	Gly	Ser	Asp	Ala	Trp	Gly	Pro	Pro	Leu	Leu	Leu	Glu
	50					55					60				
Lys	Asp	Asp	Arg	Ile	Val	Arg	Thr	Pro	Pro	Gly	Pro	Pro	Leu	Arg	Leu
65					70					75					80
Ala	Arg	Asn	Gly	Ser	His	Gln	Val	Thr	Leu	Arg	Gly	Phe	Ser	Lys	Pro
				85					90					95	
Ser	Asp	Leu	Val	Gly	Val	Phe	Ser	Cys	Val	Gly	Gly	Ala	Gly	Ala	Arg
			100					105					110		
Arg	Thr	Arg	Val	Ile	Tyr	Val	His	Asn	Ser	Pro	Gly	Ala	His	Leu	Leu
		115					120					125			
Pro	Asp	Lys	Val	Thr	His	Thr	Val	Asn	Lys	Gly	Asp	Thr	Ala	Val	Leu
	130					135					140				
Ser	Ala	Arg	Val	His	Lys	Glu	Lys	Gln	Thr	Asp	Val	Ile	Trp	Lys	Ser
145					150					155					160
Asn	Gly	Ser	Tyr	Phe	Tyr	Thr	Leu	Asp	Trp	His	Glu	Ala	Gln	Asp	Gly
				165					170					175	
Arg	Phe	Leu	Leu	Gln	Leu	Pro	Asn	Val	Gln	Pro	Pro	Ser	Ser	Gly	Ile
			180					185					190		
Tyr	Ser	Ala	Thr	Tyr	Leu	Glu	Ala	Ser	Pro	Leu	Gly	Ser	Ala	Phe	Phe
		195					200					205			
Arg	Leu	Ile	Val	Arg	Gly	Cys	Gly	Ala	Gly	Arg	Trp	Gly	Pro	Gly	Cys
	210					215					220				
Thr	Lys	Glu	Cys	Pro	Gly	Cys	Leu	His	Gly	Gly	Val	Cys	His	Asp	His
225					230					235					240
Asp	Gly	Glu	Cys	Val	Cys	Pro	Pro	Gly	Phe	Thr	Gly	Thr	Arg	Cys	Glu
				245					250					255	
Gln	Ala	Cys	Arg	Glu	Gly	Arg	Phe	Gly	Gln	Ser	Cys	Gln	Glu	Gln	Cys
			260					265					270		
Pro	Gly	Ile	Ser	Gly	Cys	Arg	Gly	Leu	Thr	Phe	Cys	Leu	Pro	Asp	Pro
		275					280					285			
Tyr	Gly	Cys	Ser	Cys	Gly	Ser	Gly	Trp	Arg	Gly	Ser	Gln	Cys	Gln	Glu
	290					295					300				
Ala	Cys	Ala	Pro	Gly	His	Phe	Gly	Ala	Asp	Cys	Arg	Leu	Gln	Cys	Gln
305					310					315					320
Cys	Gln	Asn	Gly	Gly	Thr	Cys	Asp	Arg	Phe	Ser	Gly	Cys	Val	Cys	Pro
				325					330					335	
Ser	Gly	Trp	His	Gly	Val	His	Cys	Glu	Lys	Ser	Asp	Arg	Ile	Pro	Gln
			340					345					350		
Ile	Leu	Asn	Met	Ala	Ser	Glu	Leu	Glu	Phe	Asn	Leu	Glu	Thr	Met	Pro
		355					360					365			

```
Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser
    370                 375                 380
Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Ser Thr Lys Ala
385                 390                 395                 400
Ile Val Glu Pro Glu Lys Thr Thr Ala Glu Phe Glu Val Pro Arg Leu
                405                 410                 415
Val Leu Ala Asp Ser Gly Phe Trp Glu Cys Arg Val Ser Thr Ser Gly
            420                 425                 430
Gly Gln Asp Ser Arg Arg Phe Lys Val Asn Val Lys Val Pro Pro Val
        435                 440                 445
Pro Leu Ala Ala Pro Arg Leu Leu Thr Lys Gln Ser Arg Gln Leu Val
    450                 455                 460
Val Ser Pro Leu Val Ser Phe Ser Gly Asp Gly Pro Ile Ser Thr Val
465                 470                 475                 480
Arg Leu His Tyr Arg Pro Gln Asp Ser Thr Met Asp Trp Ser Thr Ile
                485                 490                 495
Val Val Asp Pro Ser Glu Asn Val Thr Leu Met Asn Leu Arg Pro Lys
            500                 505                 510
Thr Gly Tyr Ser Val Arg Val Gln Leu Ser Arg Pro Gly Glu Gly Gly
        515                 520                 525
Glu Gly Ala Trp Gly Pro Pro Thr Leu Met Thr Thr Asp Cys Pro Glu
    530                 535                 540
Pro Leu Leu Gln Pro Trp Leu Glu Gly Trp His Val Glu Gly Thr Asp
545                 550                 555                 560
Arg Leu Arg Val Ser Trp Ser Leu Pro Leu Val Pro Gly Pro Leu Val
                565                 570                 575
Gly Asp Gly Phe Leu Leu Arg Leu Trp Asp Gly Thr Arg Gly Gln Glu
            580                 585                 590
Arg Arg Glu Asn Val Ser Ser Pro Gln Ala Arg Thr Ala Leu Leu Thr
        595                 600                 605
Gly Leu Thr Pro Gly Thr His Tyr Gln Leu Asp Val Gln Leu Tyr His
    610                 615                 620
Cys Thr Leu Leu Gly Pro Ala Ser Pro Pro Ala His Val Leu Leu Pro
625                 630                 635                 640
Pro Ser Gly Pro Pro Ala Pro Arg His Leu His Ala Gln Ala Leu Ser
                645                 650                 655
Asp Ser Glu Ile Gln Leu Thr Trp Lys His Pro Glu Ala Leu Pro Gly
            660                 665                 670
Pro Ile Ser Lys Tyr Val Val Glu Val Gln Val Ala Gly Gly Ala Gly
        675                 680                 685
Asp Pro Leu Trp Ile Asp Val Asp Arg Pro Glu Glu Thr Ser Thr Ile
    690                 695                 700
Ile Arg Gly Leu Asn Ala Ser Thr Arg Tyr Leu Phe Arg Met Arg Ala
705                 710                 715                 720
Ser Ile Gln Gly Leu Gly Asp Trp Ser Asn Thr Val Glu Glu Ser Thr
                725                 730                 735
Leu Gly Asn Gly Glu Arg Ala Gly Pro Thr Gly Pro Pro Gly Leu
            740                 745                 750
```

<210> 223
<211> 2432
<212> DNA
<213> Homo Sapiens

<400> 223

catttcgccc ggctcgaggt gcaggatgca gagcaaggtg ctgctggccg tcgccctgtg 60
gctctgcgtg gagacccggg ccgcctctgt gggtttgcct agtgtttctc ttgatctgcc 120
caggctcagc atacaaaaag acatacttac aattaaggct aatacaactc ttcaaattac 180
ttgcagggga cagagggact tggactggct ttggcccaat aatcagagtg gcagtgagca 240
aagggtggag gtgactgagt gcagcgatgg cctcttctgt aagacactca caattccaaa 300
agtgatcgga aatgacactg gagcctacaa gtgcttctac cgggaaactg acttggcctc 360
ggtcatttat gtctatgttc aagattacag atctccattt attgcttctg ttagtgacca 420
acatggagtc gtgtacatta ctgagaacaa aaacaaaact gtggtgattc catgtctcgg 480
gtccatttca aatctcaacg tgtcactttg tgcaagatac ccagaaaaga gatttgttcc 540
tgatggtaac agaatttcct gggacagcaa gaagggcttt actattccca gctacatgat 600
cagctatgct ggcatggtct tctgtgaagc aaaaattaat gatgaaagtt accagtctat 660
tatgtacata gttgtcgttg tagggtatag gatttatgat gtggttctga gtccgtctca 720
tggaattgaa ctatctgttg gagaaaagct tgtcttaaat tgtacagcaa gaactgaact 780
aaatgtgggg attgacttca actgggaata cccttcttcg aagcatcagc ataagaaact 840
tgtaaaccga gacctaaaaa cccagtctgg gagtgagatg aagaaatttt tgagcacctt 900
aactatagat ggtgtaaccc ggagtgacca aggattgtac acctgtgcag catccagtgg 960
gctgatgacc aagaagaaca gcacatttgt cagggtccat gaaaaacctt ttgttgcttt 1020
tggaagtggc atggaatctc tggtggaagc cacggtgggg gagcgtgtca gaatccctgc 1080
gaagtacctt ggttacccac ccccagaaat aaaatggtat aaaaatggaa tacccccttga 1140
gtccaatcac acaattaaag cggggcatgt actgacgatt atggaagtga gtgaaagaga 1200
cacaggaaat tacactgtca tccttaccaa tcccatttca aaggagaagc agagccatgt 1260
ggtctctctg gttgtgtatg tcccacccca gattggtgag aaatctctaa tctctcctgt 1320
ggattcctac cagtacggca ccactcaaac gctgacatgt acggtctatg ccattcctcc 1380
cccgcatcac atccactggt attggcagtt ggaggaagag tgcgccaacg agcccagcca 1440
agctgtctca gtgacaaacc catacccttg tgaagaatgg agaagtgtgg aggacttcca 1500
gggaggaaat aaaattgaag ttaataaaaa tcaatttgct ctaattgaag gaaaaaacaa 1560
aactgtaagt acccttgtta tccaagcggc aaatgtgtca gctttgtaca aatgtgaagc 1620
ggtcaacaaa gtcgggagag gagagagggt gatctccttc cacgtgacca ggggtcctga 1680
aattactttg caacctgaca tgcagcccac tgagcaggag agcgtgtctt tgtggtgcac 1740
tgcagacaga tctacgtttg agaacctcac atggtacaag cttggcccac agcctctgcc 1800
aatccatgtg ggagagttgc ccacacctgt ttgcaagaac ttggatactc tttggaaatt 1860
gaatgccacc atgttctcta atagcacaaa tgacattttg atcatggagc ttaagaatgc 1920
atccttgcag gaccaaggag actatgtctg ccttgctcaa gacaggaaga ccaagaaaag 1980
acattgcgtg gtcaggcagc tcacagtcct agagcgtgtg gcacccacga tcacaggaaa 2040
cctggagaat cagacgacaa gtattgggga aagcatcgaa gtctcatgca cggcatctgg 2100
gaatcccccc ccacagatca tgtggtttaa agataatgag acccttgtag aagactcaga 2160
gtgaggaagg aggacgaagg cctctacacc tgccaggcat gcagtgttct tggctgtgca 2220
aaagtggagg cattttttcat aatagaaggt gcccaggaaa agacgaactt ggaaatcatt 2280
attctagtag gcacggcggt gattgccatg ttcttctggc tacttcttgt catcatccta 2340
cggaccgtta agcgggccaa tggaggggaa ctgaagacag gctacttgtc catcgtcatg 2400
gatccagatg aactcccatt ggatgaacat tg 2432

<210> 224
<211> 712
<212> PRT
<213> Homo Sapiens

<400> 224
Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
 1   5   10   15
Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
            20   25   30
Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
        35   40   45
Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
    50   55   60

```
Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65                  70                  75                  80
Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
                85                  90                  95
Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
            100                 105                 110
Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
        115                 120                 125
Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
    130                 135                 140
Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145                 150                 155                 160
Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                165                 170                 175
Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
            180                 185                 190
Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
        195                 200                 205
Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220
Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225                 230                 235                 240
Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255
Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270
Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285
Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300
Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320
Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335
Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
            340                 345                 350
Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365
Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
    370                 375                 380
Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400
Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415
Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430
Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445
Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460
Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480
Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495
Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510
```

```
Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525
Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540
Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560
Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575
Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590
Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
        595                 600                 605
Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
    610                 615                 620
Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625                 630                 635                 640
Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
                645                 650                 655
Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
            660                 665                 670
Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
        675                 680                 685
Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
    690                 695                 700
Glu Thr Leu Val Glu Asp Ser Glu
705                 710
```

<210> 225
<211> 2620
<212> DNA
<213> Homo Sapiens

<400> 225

```
gcagcggccg gagatgcagc ggggcgccgc gctgtgcctg cgactgtggc tctgcctggg 60
actcctggac ggcctggtga gtggctactc catgaccccc ccgaccttga acatcacgga 120
ggagtcacac gtcatcgaca ccggtgacag cctgtccatc tcctgcaggg gacagcaccc 180
cctcgagtgg gcttggccag gagctcagga ggcgccagcc accggagaca aggacagcga 240
ggacacgggg gtggtgcgag actgcgaggg cacagacgcc aggccctact gcaaggtgtt 300
gctgctgcac gaggtacatg ccaacgacac aggcagctac gtctgctact acaagtacat 360
caaggcacgc atcgagggca ccacggccgc cagctcctac gtgttcgtga gagactttga 420
gcagccattc atcaacaagc ctgacacgct cttggtcaac aggaaggacg ccatgtgggt 480
gccctgtctg gtgtccatcc ccggcctcaa tgtcacgctg cgctcgcaaa gctcggtgct 540
gtggccagac gggcaggagg tggtgtggga tgaccggcgg ggcatgctcg tgtccacgcc 600
actgctgcac gatgccctgt acctgcagtg cgagaccacc tggggagacc aggacttcct 660
ttccaacccc ttcctggtgc acatcacagg caacgagctc tatgacatcc agctgttgcc 720
caggaagtcg ctggagctgc tggtagggga gaagctggtc ctgaactgca ccgtgtgggc 780
tgagtttaac tcaggtgtca cctttgactg ggactaccca gggaagcagg cagagcgggg 840
taagtgggtg cccgagcgac gctcccagca gacccacaca gaactctcca gcatcctgac 900
catccacaac gtcagccagc acgacctggg ctcgtatgtg tgcaaggcca acaacggcat 960
ccagcgattt cgggagagca ccgaggtcat tgtgcatgaa aatcccttca tcagcgtcga 1020
gtggctcaaa ggacccatcc tggaggccac ggcaggagac gagctggtga agctgcccgt 1080
gaagctggca gcgtaccccc cgcccgagtt ccagtggtac aaggatggaa aggcactgtc 1140
cgggcgccac agtccacatg ccctggtgct caaggaggtg acagaggcca gcacaggcac 1200
ctacaccctc gccctgtgga actccgctgc tggcctgagg cgcaacatca gcctggagct 1260
ggtggtgaat gtgccccccc agatacatga gaaggaggcc tcctccccca gcatctactc 1320
```

gcgtcacagc cgccaggccc tcacctgcac ggcctacggg gtgcccctgc ctctcagcat 1380
ccagtggcac tggcggccct ggacaccctg caagatgttt gcccagcgta gtctccggcg 1440
gcggcagcag caagacctca tgccacagtg ccgtgactgg agggcggtga ccacgcagga 1500
tgccgtgaac cccatcgaga gcctggacac ctggaccgag tttgtggagg gaaagaataa 1560
gactgtgagc aagctggtga tccagaatgc caacgtgtct gccatgtaca agtgtgtggt 1620
ctccaacaag gtgggccagg atgagcggct catctacttc tatgtgacca ccatccccga 1680
cggcttcacc atcgaatcca agccatccga ggagctacta gagggccagc cggtgctcct 1740
gagctgccaa gccgacagct acaagtacga gcatctgcgc tggtaccgcc tcaacctgtc 1800
cacgctgcac gatgcgcacg ggaacccgct tctgctcgac tgcaagaacg tgcatctgtt 1860
cgccaccccc ctggccgcca gcctggagga ggtggcacct ggggcgcgcc acgccacgct 1920
cagcctgagt atcccccgcg tcgcgcccga gcacgagggc cactatgtgt gcgaagtgca 1980
agaccggcgc agccatgaca agcactgcca caagaagtac ctgtcggtgc aggccctgga 2040
agcccctcgg ctcacgcaga acttgaccga cctcctggtg aacgtgagcg actcgctgga 2100
gatgcagtgc ttggtggccg gagcgcacgc gcccagcatc gtgtggtaca aagacgagag 2160
gctgctggag gaaaagtctg gtagggaggg tggccctggc gaagggcagg tccggaggcc 2220
cgcgaggccg acgatcccaa acccaggtgg acccgcacct ccaccccacc ccctgcagga 2280
gtcgacttgg cggactccaa ccagaagctg agcatccagc gcgtgcgcga ggaggatgcg 2340
ggacgctatc tgtgcagcgt gtgcaacgcc aagggctgcg tcaactcctc cgccagcgtg 2400
gccgtggaag gctccgagga taagggcagc atggagatcg tgatccttgt cggtaccggc 2460
gtcatcgctg tcttcttctg ggtcctcctc ctcctcatct tctgtaacat gaggaggccg 2520
gcccacgcag acatcaagac gggctacctg tccatcatca tggaccccgg ggaggtgcct 2580
ctggaggagc aatgcgaata cctgtcctac gatgccagcc 2620

<210> 226
<211> 765
<212> PRT
<213> Homo Sapiens

<400> 226
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
 1   5   10   15
Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
            20   25   30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
        35   40   45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
    50   55   60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65   70   75   80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
                85   90   95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
            100   105   110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
        115   120   125
Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
    130   135   140
Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145   150   155   160
Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
                165   170   175
Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
            180   185   190
Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
        195   200   205
Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile

```
    210                 215                 220
Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225                 230                 235                 240
Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
                245                 250                 255
Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
            260                 265                 270
Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
        275                 280                 285
Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
    290                 295                 300
Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305                 310                 315                 320
Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
                325                 330                 335
Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
            340                 345                 350
Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
        355                 360                 365
Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
    370                 375                 380
Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385                 390                 395                 400
Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
                405                 410                 415
Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
            420                 425                 430
Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
        435                 440                 445
Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr
    450                 455                 460
Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465                 470                 475                 480
Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp
                485                 490                 495
Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
            500                 505                 510
Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
        515                 520                 525
Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
    530                 535                 540
Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile
545                 550                 555                 560
Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
                565                 570                 575
Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
            580                 585                 590
Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
        595                 600                 605
Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
    610                 615                 620
Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
625                 630                 635                 640
Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
                645                 650                 655
Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
```

660 665 670
Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
675 680 685
Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
690 695 700
His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705 710 715 720
Lys Ser Gly Arg Glu Gly Gly Pro Gly Glu Gly Gln Val Arg Arg Pro
725 730 735
Ala Arg Pro Thr Ile Pro Asn Pro Gly Gly Pro Ala Pro Pro Pro His
740 745 750
Pro Leu Gln Glu Ser Thr Trp Arg Thr Pro Thr Arg Ser
755 760 765

<210> 227
<211> 3096
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM006182
<309> 2004-10-26

<400> 227
catcttgcat cagcctgtgg atgtatgcct accaccgggc tccttcacca gcaaagtgga 60
aaaagaagcg tttcacaaca aattcttctt tttgggttgg ggaaacgcag tggattatag 120
ctctgttttc ttctttccaa aactgtgcac ccctggatga aacctccatc aagggagacc 180
tacaagttgc ctggggttca gtgctctaga aagttccaag gtttgtggct tgaattattc 240
taaagaagct gaaataattg aagagaagca gaggccagct gtttttgagg atcctgctcc 300
acagagaatg ctctgcaccc gttgatactc cagttccaac accatcttct gagatgatcc 360
tgattcccag aatgctcttg gtgctgttcc tgctgctgcc tatcttgagt tctgcaaaag 420
ctcaggttaa tccagctata tgccgctatc ctctgggcat gtcaggaggc cagattccag 480
atgaggacat cacagcttcc agtcagtggt cagagtccac agctgccaaa tatggaaggc 540
tggactcaga agaaggggat ggagcctggt gccctgagat tccagtggaa cctgatgacc 600
tgaaggagtt tctgcagatt gacttgcaca ccctccattt tatcactctg gtggggaccc 660
aggggcgcca tgcaggaggt catggcatcg agtttgcccc catgtacaag atcaattaca 720
gtcgggatgg cactcgctgg atctcttggc ggaaccgtca tgggaaacag gtgctggatg 780
gaaatagtaa cccctatgac attttcctaa aggacttgga gccgcccatt gtagccagat 840
ttgtccggtt cattccagtc accgaccact ccatgaatgt gtgtatgaga gtggagcttt 900
acggctgtgt ctggctagat ggcttggtgt cttacaatgc tccagctggg cagcagtttg 960
tactccctgg aggttccatc atttatctga atgattctgt ctatgatgga gctgttggat 1020
acagcatgac agaagggcta ggccaattga ccgatggtgt gtctggcctg gacgatttca 1080
cccagaccca tgaataccac gtgtggcccg gctatgacta tgtgggctgg cggaacgaga 1140
gtgccaccaa tggctacatt gagatcatgt ttgaatttga ccgcatcagg aatttcacta 1200
ccatgaaggt ccactgcaac aacatgtttg ctaaaggtgt gaagatcttt aaggaggtac 1260
agtgctactt ccgctctgaa gccagtgagt gggaacctaa tgccatttcc ttccccctg 1320
tcctggatga cgtcaacccc agtgctcggt ttgtcacggt gcctctccac caccgaatgg 1380
ccagtgccat caagtgtcaa taccattttg cagatacctg gatgatgttc agtgagatca 1440
ccttccaatc agatgctgca atgtacaaca actctgaagc cctgcccacc tctcctatgg 1500
cacccacaac ctatgatcca atgcttaaag ttgatgacag caacactcgg atcctgattg 1560
gctgcttggt ggccatcatc tttatcctcc tggccatcat tgtcatcatc ctctggaggc 1620
agttctggca gaaaatgctg gagaaggctt ctcggaggat gctggatgat gaaatgacag 1680
tcagcctttc cctgccaagt gattctagca tgttcaacaa taaccgctcc tcatcaccta 1740
gtgaacaagg gtccaactcg acttacgatc gcatctttcc ccttcgccct gactaccagg 1800
agccatccag gctgatacga aaactcccag aatttgctcc aggggaggag gagtcaggct 1860

gcagcggtgt tgtgaagcca gtccagccca gtggccctga gggggtgccc cactatgcag 1920
aggctgacat agtgaacctc caaggagtga caggaggcaa cacatactca gtgcctgccg 1980
tcaccatgga cctgctctca ggaaaagatg tggctgtgga ggagttcccc aggaaactcc 2040
taactttcaa agagaagctg ggagaaggac agtttgggga ggttcatctc tgtgaagtgg 2100
agggaatgga aaaattcaaa gacaaagatt ttgccctaga tgtcagtgcc aaccagcctg 2160
tcctggtggc tgtgaaaatg ctccgagcag atgccaacaa gaatgccagg aatgattttc 2220
ttaaggagat aaagatcatg tctcggctca aggacccaaa catcatccat ctattatctg 2280
tgtgtatcac tgatgaccct ctctgtatga tcactgaata catggagaat ggagatctca 2340
atcagtttct ttcccgccac gagcccccta attcttcctc cagcgatgta cgcactgtca 2400
gttacaccaa tctgaagttt atggctaccc aaattgcctc tggcatgaag tacctttcct 2460
ctcttaattt tgttcaccga gatctggcca cacgaaactg tttagtgggt aagaactaca 2520
caatcaagat agctgacttt ggaatgagca ggaacctgta cagtggtgac tattaccgga 2580
tccagggccg ggcagtgctc cctatccgct ggatgtcttg ggagagtatc ttgctgggca 2640
agttcactac agcaagtgat gtgtgggcct ttggggttac tttgtgggag actttcacct 2700
tttgtcaaga acagccctat tcccagctgt cagatgaaca ggttattgag aatactggag 2760
agttcttccg agaccaaggg aggcagactt acctccctca accagccatt tgtcctgact 2820
ctgtgtataa gctgatgctc agctgctgga gaagagatac gaagaaccgt ccctcattcc 2880
aagaaatcca ccttctgctc cttcaacaag gcgacgagtg atgctgtcag tgcctggcca 2940
tgttcctacg gctcaggtcc tccctacaag acctaccact cacccatgcc tatgccactc 3000
catctggaca tttaatgaaa ctgagagaca gaggcttgtt tgctttgccc tcttttcctg 3060
gtcaccccca ctccctaccc ctgactcata tatact 3096

<210> 228
<211> 5616
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM005228
<309> 2005-01-26

<400> 228
ccccggcgca gcgcggccgc agcagcctcc gccccccgca cggtgtgagc gcccgacgcg 60
gccgaggcgg ccggagtccc gagctagccc cggcggccgc cgccgcccag accggacgac 120
aggccacctc gtcggcgtcc gcccgagtcc ccgcctcgcc gccaacgcca caaccaccgc 180
gcacggcccc ctgactccgt ccagtattga tcgggagagc cggagcgagc tcttcgggga 240
gcagcgatgc gaccctccgg gacggccggg gcagcgctcc tggcgctgct ggctgcgctc 300
tgcccggcga gtcgggctct ggaggaaaag aaagtttgcc aaggcacgag taacaagctc 360
acgcagttgg gcacttttga agatcatttt ctcagcctcc agaggatgtt caataactgt 420
gaggtggtcc ttgggaattt ggaaattacc tatgtgcaga ggaattatga tctttccttc 480
ttaaagacca tccaggaggt ggctggttat gtcctcattg ccctcaacac agtggagcga 540
attcctttgg aaaacctgca gatcatcaga ggaaatatgt actacgaaaa ttcctatgcc 600
ttagcagtct tatctaacta tgatgcaaat aaaaccggac tgaaggagct gcccatgaga 660
aatttacagg aaatcctgca tggcgccgtg cggttcagca acaaccctgc cctgtgcaac 720
gtggagagca tccagtggcg ggacatagtc agcagtgact ttctcagcaa catgtcgatg 780
gacttccaga accacctggg cagctgccaa aagtgtgatc caagctgtcc caatgggagc 840
tgctggggtg caggagagga gaactgccag aaactgacca aaatcatctg tgcccagcag 900
tgctccgggc gctgccgtgg caagtccccc agtgactgct gccacaacca gtgtgctgca 960
ggctgcacag gcccccggga gagcgactgc ctggtctgcc gcaaattccg agacgaagcc 1020
acgtgcaagg acacctgccc cccactcatg ctctacaacc ccaccacgta ccagatggat 1080
gtgaaccccg agggcaaata cagctttggt gccacctgcg tgaagaagtg tccccgtaat 1140
tatgtggtga cagatcacgg ctcgtgcgtc cgagcctgtg gggccgacag ctatgagatg 1200
gaggaagacg gcgtccgcaa gtgtaagaag tgcgaagggc cttgccgcaa agtgtgtaac 1260
ggaataggta ttggtgaatt taaagactca ctctccataa atgctacgaa tattaaacac 1320
ttcaaaaact gcacctccat cagtggcgat ctccacatcc tgccggtggc atttaggggt 1380
gactccttca cacatactcc tcctctggat ccacaggaac tggatattct gaaaaccgta 1440

aaggaaatca cagggttttt gctgattcag gcttggcctg aaaacaggac ggacctccat 1500
gcctttgaga acctagaaat catacgcggc aggaccaagc aacatggtca gttttctctt 1560
gcagtcgtca gcctgaacat aacatccttg ggattacgct ccctcaagga gataagtgat 1620
ggagatgtga taatttcagg aaacaaaaat ttgtgctatg caaatacaat aaactggaaa 1680
aaactgtttg ggacctccgg tcagaaaacc aaaattataa gcaacagagg tgaaaacagc 1740
tgcaaggcca caggccaggt ctgccatgcc ttgtgctccc ccgagggctg ctggggcccg 1800
gagcccaggg actgcgtctc ttgccggaat gtcagccgag gcagggaatg cgtggacaag 1860
tgcaaccttc tggagggtga gccaagggag tttgtggaga actctgagtg catacagtgc 1920
cacccagagt gcctgcctca ggccatgaac atcacctgca caggacgggg accagacaac 1980
tgtatccagt gtgcccacta cattgacggc ccccactgcg tcaagacctg cccggcagga 2040
gtcatgggag aaaacaacac cctggtctgg aagtacgcag acgccggcca tgtgtgccac 2100
ctgtgccatc caaactgcac ctacggatgc actgggccag gtcttgaagg ctgtccaacg 2160
aatgggccta agatcccgtc catcgccact gggatggtgg gggccctcct cttgctgctg 2220
gtggtggccc tggggatcgg cctcttcatg cgaaggcgcc acatcgttcg gaagcgcacg 2280
ctgcggaggc tgctgcagga gagggagctt gtggagcctc ttacacccag tggagaagct 2340
cccaaccaag ctctcttgag gatcttgaag gaaactgaat tcaaaaagat caaagtgctg 2400
ggctccggtg cgttcggcac ggtgtataag ggactctgga tcccagaagg tgagaaagtt 2460
aaaattcccg tcgctatcaa ggaattaaga gaagcaacat ctccgaaagc caacaaggaa 2520
atcctcgatg aagcctacgt gatggccagc gtggacaacc cccacgtgtg ccgcctgctg 2580
ggcatctgcc tcacctccac cgtgcagctc atcacgcagc tcatgccctt cggctgcctc 2640
ctggactatg tccgggaaca caaagacaat attggctccc agtacctgct caactggtgt 2700
gtgcagatcg caaagggcat gaactacttg gaggaccgtc gcttggtgca ccgcgacctg 2760
gcagccagga acgtactggt gaaaacaccg cagcatgtca agatcacaga ttttgggctg 2820
gccaaactgc tgggtgcgga agagaaagaa taccatgcag aaggaggcaa agtgcctatc 2880
aagtggatgg cattggaatc aattttacac agaatctata cccaccagag tgatgtctgg 2940
agctacgggg tgaccgtttg ggagttgatg acctttggat ccaagccata tgacggaatc 3000
cctgccagcg agatctcctc catcctggag aaaggagaac gcctccctca gccacccata 3060
tgtaccatcg atgtctacat gatcatggtc aagtgctgga tgatagacgc agatagtcgc 3120
ccaaagttcc gtgagttgat catcgaattc tccaaaatgg cccgagaccc ccagcgctac 3180
cttgtcattc agggggatga aagaatgcat ttgccaagtc ctacagactc caacttctac 3240
cgtgccctga tggatgaaga agacatggac gacgtggtgg atgccgacga gtacctcatc 3300
ccacagcagg gcttcttcag cagcccctcc acgtcacgga ctcccctcct gagctctctg 3360
agtgcaacca gcaacaattc caccgtggct tgcattgata gaaatgggct gcaaagctgt 3420
cccatcaagg aagacagctt cttgcagcga tacagctcag accccacagg cgccttgact 3480
gaggacagca tagacgacac cttcctccca gtgcctgaat acataaacca gtccgttccc 3540
aaaaggcccg ctggctctgt gcagaatcct gtctatcaca atcagcctct gaaccccgcg 3600
cccagcagag acccacacta ccaggacccc cacagcactg cagtgggcaa ccccgagtat 3660
ctcaacactg tccagcccac ctgtgtcaac agcacattcg acagccctgc ccactgggcc 3720
cagaaaggca gccaccaaat tagcctggac aaccctgact accagcagga cttctttccc 3780
aaggaagcca agccaaatgg catctttaag ggctccacag ctgaaaatgc agaataccta 3840
agggtcgcgc cacaaagcag tgaatttatt ggagcatgac cacggaggat agtatgagcc 3900
ctaaaaatcc agactctttc gatacccagg accaagccac agcaggtcct ccatcccaac 3960
agccatgccc gcattagctc ttagacccac agactggttt tgcaacgttt acaccgacta 4020
gccaggaagt acttccacct cgggcacatt ttgggaagtt gcattccttt gtcttcaaac 4080
tgtgaagcat ttacagaaac gcatccagca agaatattgt ccctttgagc agaaatttat 4140
ctttcaaaga ggtatatttg aaaaaaaaaa aaagtatatg tgaggatttt tattgattgg 4200
ggatcttgga gtttttcatt gtcgctattg atttttactt caatgggctc ttccaacaag 4260
gaagaagctt gctggtagca cttgctaccc tgagttcatc caggcccaac tgtgagcaag 4320
gagcacaagc cacaagtctt ccagaggatg cttgattcca gtggttctgc ttcaaggctt 4380
ccactgcaaa acactaaaga tccaagaagg ccttcatggc cccagcaggc cggatcggta 4440
ctgtatcaag tcatggcagg tacagtagga taagccactc tgtcccttcc tgggcaaaga 4500
agaaacggag gggatggaat tcttccttag acttactttt gtaaaaatgt ccccacggta 4560
cttactcccc actgatggac cagtggtttc cagtcatgag cgttagactg acttgtttgt 4620
cttccattcc attgttttga aactcagtat gctgcccctg tcttgctgtc atgaaatcag 4680
caagagagga tgacacatca aataataact cggattccag cccacattgg attcatcagc 4740
atttggacca atagcccaca gctgagaatg tggaatacct aaggatagca ccgcttttgt 4800

tctcgcaaaa acgtatctcc taatttgagg ctcagatgaa atgcatcagg tcctttgggg 4860
catagatcag aagactacaa aaatgaagct gctctgaaat ctcctttagc catcacccca 4920
acccccccaaa attagtttgt gttacttatg gaagatagtt ttctcctttt acttcacttc 4980
aaaagctttt tactcaaaga gtatatgttc cctccaggtc agctgccccc aaaccccctc 5040
cttacgcttt gtcacacaaa aagtgtctct gccttgagtc atctattcaa gcacttacag 5100
ctctggccac aacagggcat tttacaggtg cgaatgacag tagcattatg agtagtgtgg 5160
aattcaggta gtaaatatga aactagggtt tgaaattgat aatgctttca caacatttgc 5220
agatgtttta gaaggaaaaa agttccttcc taaaataatt tctctacaat tggaagattg 5280
gaagattcag ctagttagga gcccaccttt tttcctaatc tgtgtgtgcc ctgtaacctg 5340
actggttaac agcagtcctt tgtaaacagt gttttaaact ctcctagtca atatccaccc 5400
catccaattt atcaaggaag aaatggttca gaaaatattt tcagcctaca gttatgttca 5460
gtcacacaca catacaaaat gttccttttg cttttaaagt aatttttgac tcccagatca 5520
gtcagagccc ctacagcatt gttaagaaag tatttgattt ttgtctcaat gaaaataaaa 5580
ctatattcat ttccactcta aaaaaaaaaa aaaaaa 5616

<210> 229
<211> 3963
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004431
<309> 2004-12-20

<400> 229
attaaggact cggggcagga ggggcagaag ttgcgcgcag gccggcgggc gggagcggac 60
accgaggccg gcgtgcaggc gtgcgggtgt gcgggagccg ggctcggggg gatcggaccg 120
agagcgagaa gcgcggcatg gagctccagg cagcccgcgc ctgcttcgcc ctgctgtggg 180
gctgtgcgct ggccgcggcc gcggcggcgc agggcaagga agtggtactg ctggactttg 240
ctgcagctgg aggggagctc ggctggctca cacacccgta tggcaaaggg tgggacctga 300
tgcagaacat catgaatgac atgccgatct acatgtactc cgtgtgcaac gtgatgtctg 360
gcgaccagga caactggctc cgcaccaact gggtgtaccg aggagaggct gagcgtatct 420
tcattgagct caagtttact gtacgtgact gcaacagctt ccctggtggc gccagctcct 480
gcaaggagac tttcaacctc tactatgccg agtcggacct ggactacggc accaacttcc 540
agaagcgcct gttcaccaag attgacacca ttgcgcccga tgagatcacc gtcagcagcg 600
acttcgaggc acgccacgtg aagctgaacg tggaggagcg ctccgtgggg ccgctcaccc 660
gcaaaggctt ctacctggcc ttccaggata tcggtgcctg tgtggcgctg ctctccgtcc 720
gtgtctacta caagaagtgc cccgagctgc tgcagggcct ggcccacttc cctgagacca 780
tcgccggctc tgatgcacct tccctggcca ctgtggccgg cacctgtgtg gaccatgccg 840
tggtgccacc ggggggtgaa gagccccgta tgcactgtgc agtggatggc gagtggctgg 900
tgcccattgg gcagtgcctg tgccaggcag gctacgagaa ggtggaggat gcctgccagg 960
cctgctcgcc tggatttttt aagtttgagg catctgagag cccctgcttg gagtgccctg 1020
agcacacgct gccatcccct gagggtgcca cctcctgcga gtgtgaggaa ggcttcttcc 1080
gggcacctca ggacccagcg tcgatgcctt gcacacgacc cccctccgcc ccacactacc 1140
tcacagccgt gggcatgggt gccaaggtgg agctgcgctg gacgccccct caggacagcg 1200
ggggccgcga ggacattgtc tacagcgtca cctgcgaaca gtgctggccc gagtctgggg 1260
aatgcgggcc gtgtgaggcc agtgtgcgct actcggagcc tcctcacgga ctgacccgca 1320
ccagtgtgac agtgagcgac ctggagcccc acatgaacta caccttcacc gtggaggccc 1380
gcaatggcgt ctcaggcctg gtaaccagcc gcagcttccg tactgccagt gtcagcatca 1440
accagacaga gccccccaag gtgaggctgg agggccgcag caccacctcg cttagcgtct 1500
cctggagcat ccccccgccg cagcagagcc gagtgtggaa gtacgaggtc acttaccgca 1560
agaagggaga ctccaacagc tacaatgtgc gccgcaccga gggtttctcc gtgaccctgg 1620
acgacctggc cccagacacc acctacctgg tccaggtgca ggcactgacg caggagggcc 1680
agggggccgg cagcaaggtg cacgaattcc agacgctgtc cccggaggga tctggcaact 1740

tggcggtgat tggcggcgtg gctgtcggtg tggtcctgct tctggtgctg gcaggagttg 1800
gcttctttat ccaccgcagg aggaagaacc agcgtgcccg ccagtccccg gaggacgttt 1860
acttctccaa gtcagaacaa ctgaagcccc tgaagacata cgtggacccc cacacatatg 1920
aggaccccaa ccaggctgtg ttgaagttca ctaccgagat ccatccatcc tgtgtcactc 1980
ggcagaaggt gatcggagca ggagagtttg gggaggtgta caagggcatg ctgaagacat 2040
cctcggggaa gaaggaggtg ccggtggcca tcaagacgct gaaagccggc tacacagaga 2100
agcagcgagt ggacttcctc ggcgaggccg gcatcatggg ccagttcagc caccacaaca 2160
tcatccgcct agagggcgtc atctccaaat acaagcccat gatgatcatc actgagtaca 2220
tggagaatgg ggccctggac aagttccttc gggagaagga tggcgagttc agcgtgctgc 2280
agctggtggg catgctgcgg ggcatcgcag ctggcatgaa gtacctggcc aacatgaact 2340
atgtgcaccg tgacctggct gcccgcaaca tcctcgtcaa cagcaacctg gtctgcaagg 2400
tgtctgactt tggcctgtcc cgcgtgctgg aggacgaccc cgaggccacc tacaccacca 2460
gtggcggcaa gatccccatc cgctggaccg ccccggaggc catttcctac cggaagttca 2520
cctctgccag cgacgtgtgg agctttggca ttgtcatgtg ggaggtgatg acctatggcg 2580
agcggcccta ctgggagttg tccaaccacg aggtgatgaa agccatcaat gatggcttcc 2640
ggctccccac acccatggac tgcccctccg ccatctacca gctcatgatg cagtgctggc 2700
agcaggagcg tgcccgccgc cccaagttcg ctgacatcgt cagcatcctg gacaagctca 2760
ttcgtgcccc tgactccctc aagaccctgg ctgactttga cccccgcgtg tctatccggc 2820
tccccagcac gagcggctcg gaggggggtgc ccttccgcac ggtgtccgag tggctggagt 2880
ccatcaagat gcagcagtat acggagcact tcatggcggc cggctacact gccatcgaga 2940
aggtggtgca gatgaccaac gacgacatca agaggattgg ggtgcggctg cccggccacc 3000
agaagcgcat cgcctacagc ctgctgggac tcaaggacca ggtgaacact gtggggatcc 3060
ccatctgagc ctcgacaggg cctggagccc catcggccaa gaatacttga agaaacagag 3120
tggcctccct gctgtgccat gctgggccac tggggacttt atttatttct agttctttcc 3180
tccccctgca acttccgctg aggggtctcg gatgacaccc tggcctgaac tgaggagatg 3240
accagggatg ctgggctggg ccctctttcc ctgcgagacg cacacagctg agcacttagc 3300
aggcaccgcc acgtcccagc atccctggag caggagcccc gccacagcct tcggacagac 3360
atataggata ttcccaagcc gaccttccct ccgccttctc ccacatgagg ccatctcagg 3420
agatggaggg cttggcccag cgccaagtaa acagggtacc tcaagcccca tttcctcaca 3480
ctaagagggc agactgtgaa cttgactggg tgagacccaa agcggtccct gtccctctag 3540
tgccttcttt agaccctcgg gccccatcct catccctgac tggccaaacc cttgctttcc 3600
tgggcctttg caagatgctt ggttgtgttg aggtttttaa atatatattt tgtactttgt 3660
ggagagaatg tgtgtgtgtg gcagggggcc ccgccagggc tggggacaga gggtgtcaaa 3720
cattcgtgag ctggggactc agggaccggt gctgcaggag tgtcctgccc atgccccagt 3780
cggccccatc tctcatcctt ttggataagt ttctattctg tcagtgttaa agattttgtt 3840
ttgttggaca tttttttcga atcttaattt attatttttt ttatatttat tgttagaaaa 3900
tgacttattt ctgctctgga ataaagttgc agatgattca aaccgaaaaa aaaaaaaaaa 3960
aaa 3963

<210> 230
<211> 5826
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM005233
<309> 2004-11-16

<400> 230
cccgctctgc ttcagcgcac gctgaagacg gcactaggac ccagggaagt ccccgagcgg 60
ggttcgcgga aaggcagcca gactcctcct tatctccagt gtcaaacttg acatcagcct 120
gcgagcggag catggtaact tctccagcaa tcagagcgct ccccctcaca tcagtggcat 180
gcttcatgga gatatgctcc tctcactgcc ctctgcacca gcaacatgga ttgtcagctc 240
tccatcctcc tccttctcag ctgctctgtt ctcgacagct tcggggaact gattccgcag 300
ccttccaatg aagtcaatct actggattca aaaacaattc aaggggagct gggctggatc 360
tcttatccat cacatgggtg ggaagagatc agtggtgtgg atgaacatta cacacccatc 420

aggacttacc aggtgtgcaa tgtcatggac cacagtcaaa acaattggct gagaacaaac 480
tgggtcccca ggaactcagc tcagaagatt tatgtggagc tcaagttcac tctacgagac 540
tgcaatagca ttccattggt tttaggaact tgcaaggaga cattcaacct gtactacatg 600
gagtctgatg atgatcatgg ggtgaaattt cgagagcatc agtttacaaa gattgacacc 660
attgcagctg atgaaagttt cactcaaatg gatcttgggg accgtattct gaagctcaac 720
actgagatta gagaagtagg tcctgtcaac aagaagggat tttatttggc atttcaagat 780
gttggtgctt gtgttgcctt ggtgtctgtg agagtatact tcaaaaagtg cccatttaca 840
gtgaagaatc tggctatgtt tccagacacg gtacccatgg actcccagtc cctggtggag 900
gttagagggt cttgtgtcaa caattctaag gaggaagatc ctccaaggat gtactgcagt 960
acagaaggcg aatggcttgt acccattggc aagtgttcct gcaatgctgg ctatgaagaa 1020
agaggtttta tgtgccaagc ttgtcgacca ggtttctaca aggcattgga tggtaatatg 1080
aagtgtgcta agtgcccgcc tcacagttct actcaggaag atggttcaat gaactgcagg 1140
tgtgagaata attacttccg ggcagacaaa gaccctccat ccatggcttg tacccgacct 1200
ccatcttcac caagaaatgt tatctctaat ataaacgaga cctcagttat cctggactgg 1260
agttggcccc tggacacagg aggccggaaa gatgttacct tcaacatcat atgtaaaaaa 1320
tgtgggtgga atataaaaca gtgtgagcca tgcagcccaa atgtccgctt cctccctcga 1380
cagtttggac tcaccaacac cacggtgaca gtgacagacc ttctggcaca tactaactac 1440
acctttgaga ttgatgccgt taatggggtg tcagagctga gctccccacc aagacagttt 1500
gctgcggtca gcatcacaac taatcaggct gctccatcac ctgtcctgac gattaagaaa 1560
gatcggacct ccagaaatag catctctttg tcctggcaag aacctgaaca tcctaatggg 1620
atcatattgg actacgaggt caaatactat gaaaagcagg aacaagaaac aagttatacc 1680
attctgaggg caagaggcac aaatgttacc atcagtagcc tcaagcctga cactatatac 1740
gtattccaaa tccgagcccg aacagccgct ggatatggga cgaacagccg caagtttgag 1800
tttgaaacta gtccagactc tttctccatc tctggtgaaa gtagccaagt ggtcatgatc 1860
gccatttcag cggcagtagc aattattctc ctcactgttg tcatctatgt tttgattggg 1920
aggttctgtg gctataagtc aaaacatggg gcagatgaaa aaagacttca ttttggcaat 1980
gggcatttaa aacttccagg tctcaggact tatgttgacc cacatacata tgaagaccct 2040
acccaagctg ttcatgagtt tgccaaggaa ttggatgcca ccaacatatc cattgataaa 2100
gttgttggag caggtgaatt tggagaggtg tgcagtggtc gcttaaaact tccttcaaaa 2160
aaagagattt cagtggccat taagaccctg aaagttggct acacagaaaa gcagaggaga 2220
gacttcctgg gagaagcaag cattatggga cagtttgacc accccaatat cattcgactg 2280
gaaggagttg ttaccaaaag taagccagtt atgattgtca cagaatacat ggagaatggt 2340
tccttggata gtttcctacg taaacacgat gcccagttta ctgtcattca gctagtgggg 2400
atgcttcgag ggatagcatc tggcatgaag tacctgtcag acatgggcta tgttcaccga 2460
gacctcgctg ctcggaacat cttgatcaac agtaacttgg tgtgtaaggt ttctgatttc 2520
ggactttcgc gtgtcctgga ggatgaccca gaagctgctt atacaacaag aggagggaag 2580
atcccaatca ggtggacatc accagaagct atagcctacc gcaagttcac gtcagccagc 2640
gatgtatgga gttatgggat tgttctctgg gaggtgatgt cttatggaga gagaccatac 2700
tgggagatgt ccaatcagga tgtaattaaa gctgtagatg agggctatcg actgccaccc 2760
cccatggact gcccagctgc cttgtatcag ctgatgctgg actgctggca gaaagacagg 2820
aacaacagac ccaagtttga gcagattgtt agtattctgg acaagcttat ccggaatccc 2880
ggcagcctga agatcatcac cagtgcagcc gcaaggccat caaaccttct tctggaccaa 2940
agcaatgtgg atatcactac cttccgcaca acaggtgact ggcttaatgg tgtctggaca 3000
gcacactgca aggaaatctt cacgggtgtg gagtacagtt cttgtgacac aatagccaag 3060
atttccacag atgacatgaa aaaggttggt gtcaccgtgg ttgggccaca gaagaagatc 3120
atcagtagca ttaaagctct agaaacgcaa tcaaagaatg gcccagttcc cgtgtaaagc 3180
acgggacgga agtgcttctg gacggaagtg gtggctgtgg aaggcgtagc atcatcctgc 3240
agacagacaa taattctgga gatactggtg gaagttccaa gtccaataag acactcaaat 3300
atgagtacaa atgccttaaa atggaattga aaaactcttt attttcccct atcatttatt 3360
ggatgggtgg gtggggtatt tttttgtaat tgctttttta aatattagtt aatggattaa 3420
atttaattct tcagcgtaaa atggtgaaga actagcatat agccattgat cataaactga 3480
ctatcataaa atcaaaacaa gtgaaataac aaaatggaca tggtggcttt gtttaggtag 3540
agccacaaaa gaaaagactt gtaatatttt tatatacaga ggaaatctgt aacaggtatt 3600
ttgtttcttt taaagcaagc aacacagagg aatttatacc tcaaactatc tggccatatt 3660
tactacctta tcactgcatt attctctttt atctgtttaa agcatataga gatgaagttt 3720
gtagttgttt taagtactac acatttttaa attgttagct tccttaagta tatcatgtaa 3780

agaaatgtct taatttttga aaaaagtaca tatttatttt cttttgaatt gtttttattg 3840
ttttctattt atgccttgat gatttaatat ggatttgtta cagccaagtg ccaaatgctc 3900
tctcaaattg tcagcaattt aactagacac agataataat gggtttcttt cagatttttt 3960
gaaccatcca cttacatata tttttaaaaa atgaaatcct tttcctgttc atacactaac 4020
caaatctctc aaatctgtta tcccaatcat tgttgcctct ccgtttatta taaactgtat 4080
gctcacaact tagtgtaata taccagcttg tatgcaatgg attttcaacc agataacata 4140
cctttcctgc tctggtgctt agagactatc aactccctcc tttagtgaag gagccgtgtt 4200
agagcttccg agaatagctc cactggagag aagtggaatc ctatatagaa tgctgcacta 4260
attgacaaca cagcctatag gccaatgcat gagtaaaaaa aaaaacaatt actggctcac 4320
tggctttgaa aagtcactta ctattgttgc tgaaacttgc tgagctgttt atagagaatg 4380
atgataacag aacttttcct ctgtatcact ggtgtttagg tgaattaatt aaacattgtg 4440
atcattagta ccaggtatta ttatctttaa gagtcttcca cttcaatgca catggtgcag 4500
ttttggtgtg taacttagaa ggattgaact tctttgaatt tactggacat aacattttca 4560
gaatagttgg tcatctagca accgcctcaa aatgtgtaag caggagagaa atttctcatc 4620
acagggattt agacttacta ttacataaag gctaactatg agcttgctca ttaattttga 4680
aaagatgtac ctggtggata tctagctagt aatatattct gaagcaacat tttagctcta 4740
ttgatactct ttctaatgct gatatgatct tgagtataag aaatgcatat gtcactagaa 4800
tggataaaat aatgctgcaa acttaatgtt cttatgcaaa atggaacgct aatgaaacac 4860
agcttacaat cgcaaatcaa aactcacaag tgctcatctg ttgtagattt agtgtaataa 4920
gacttagatt gtgctccttc ggatatgatt gtttctcaaa tcttggcaat attccttagt 4980
caaatcaggc tactagaatt ctgtattgga tatataagag catgaaattt ttaaaaatac 5040
acttgtgatt ataaaattaa tcacaaattt cacttatacc tgctatcagc agctagaaaa 5100
catttttttt ttaaatcaag tattttgtgt ttggaatgtt agaatgagat ctgaatgtgg 5160
tttcaatcta attttttccc agactactat tttctttttt aggtactatt ctgagcatac 5220
tcaacaaaac ccatgcattt cataaactaa tagaagttga ggattgttga atctatttca 5280
cttattttgg ctgtggtttc catctgaaag tagaggttgt atacaccata tactgttctt 5340
cattttatta atatttttct ccttgacctc tcataaattt actttacaca attcttaccc 5400
tgtacatatg taaacataag tgtacgattc ttaaccatgg agtagaggta ctagaatgct 5460
tacggccatc tctttgtaca ggaactgcat tgactttcag taaacataaa gccacaactc 5520
ctacatgatg ttatgtacca tatgatctgt tttgtatctt aaatttgatt tacatatatt 5580
atttatttct ggtaactcac tcagtttatg ctgtgctaaa tatcaatcaa gccatgtata 5640
aatgtgatat gattggcaat atgtgtttac tttaaacttg tcttttcaaa atattactca 5700
gtttatgttg tacaatgtag atggcctctt actaatgtaa aatgatttgt agtggaaaca 5760
tttatatttt tataataaac ataatgaaaa tatttttttac agattggaaa aaaaaaaaaa 5820
aaaaaa 5826

<210> 231
<211> 6364
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004438
<309> 2004-11-16

<400> 231
ctgggataga agcggcagga gcagcgttgg caccggcgaa ccatggctgg gattttctat 60
ttcgccctat tttcgtgtct cttcgggatt tgcgacgctg tcacaggttc cagggtatac 120
cccgcgaatg aagttacctt attggattcc agatctgttc agggagaact tgggtggata 180
gcaagccctc tggaaggagg gtgggaggaa gtgagtatca tggatgaaaa aaatacacca 240
atccgaacct accaagtgtg caatgtgatg gaacccagcc agaataactg gctacgaact 300
gattggatca cccgagaagg ggctcagagg gtgtatattg agattaaatt caccttgagg 360
gactgcaata gtcttccggg cgtcatgggg acttgcaagg agacgtttaa cctgtactac 420
tatgaatcag acaacgacaa agagcgtttc atcagagaga accagtttgt caaaattgac 480

accattgctg ctgatgagag cttcacccaa gtggacattg gtgacagaat catgaagctg 540
aacaccgaga tccgggatgt agggccatta agcaaaaagg ggttttacct ggcttttcag 600
gatgtggggg cctgcatcgc cctggtatca gtccgtgtgt tctataaaaa gtgtccactc 660
acagtccgca atctggccca gtttcctgac accatcacag gggctgatac gtcttccctg 720
gtggaagttc gaggctcctg tgtcaacaac tcagaagaga aagatgtgcc aaaaatgtac 780
tgtggggcag atggtgaatg gctggtaccc attggcaact gcctatgcaa cgctgggcat 840
gaggagcgga gcggagaatg ccaagcttgc aaaattggat attacaaggc tctctccacg 900
gatgccacct gtgccaagtg cccaccccac agctactctg tctgggaagg agccacctcg 960
tgcacctgtg accgaggctt tttcagagct gacaacgatg ctgcctctat gccctgcacc 1020
cgtccaccat ctgctcccct gaacttgatt tcaaatgtca acgagacatc tgtgaacttg 1080
gaatggagta gccctcagaa tacaggtggc cgccaggaca tttcctataa tgtggtatgc 1140
aagaaatgtg gagctggtga ccccagcaag tgccgaccct gtggaagtgg ggtccactac 1200
accccacagc agaatggctt gaagaccacc aaagtctcca tcactgacct cctagctcat 1260
accaattaca cctttgaaat ctgggctgtg aatggagtgt ccaaatataa ccctaaccca 1320
gaccaatcag tttctgtcac tgtgaccacc aaccaagcag caccatcatc cattgctttg 1380
gtccaggcta aagaagtcac aagatacagt gtggcactgg cttggctgga accagatcgg 1440
cccaatgggg taatcctgga atatgaagtc aagtattatg agaaggatca gaatgagcga 1500
agctatcgta tagttcggac agctgccagg aacacagata tcaaaggcct gaaccctctc 1560
acttcctatg ttttccacgt gcgagccagg acagcagctg gctatggaga cttcagtgag 1620
cccttggagg ttacaaccaa cacagtgcct tcccggatca ttggagatgg ggctaactcc 1680
acagtccttc tggtctctgt ctcgggcagt gtggtgctgg tggtaattct cattgcagct 1740
tttgtcatca gccggagacg gagtaaatac agtaaagcca aacaagaagc ggatgaagag 1800
aaacatttga atcaaggtgt aagaacatat gtggacccct ttacgtacga agatcccaac 1860
caagcagtgc gagagtttgc caaagaaatt gacgcatcct gcattaagat tgaaaaagtt 1920
ataggagttg gtgaatttgg tgaggtatgc agtgggcgtc tcaaagtgcc tggcaagaga 1980
gagatctgtg tggctatcaa gactctgaaa gctggttata cagacaaaca gaggagagac 2040
ttcctgagtg aggccagcat catgggacag tttgaccatc cgaacatcat tcacttggaa 2100
ggcgtggtca ctaaatgtaa accagtaatg atcataacag agtacatgga gaatggctcc 2160
ttggatgcat tcctcaggaa aaatgatggc agatttacag tcattcagct ggtgggcatg 2220
cttcgtggca ttgggtctgg gatgaagtat ttatctgata tgagctatgt gcatcgtgat 2280
ctggccgcac ggaacatcct ggtgaacagc aacttggtct gcaaagtgtc tgattttggc 2340
atgtcccgag tgcttgagga tgatccggaa gcagcttaca ccaccagggg tggcaagatt 2400
cctatccggt ggactgcgcc agaagcaatt gcctatcgta aattcacatc agcaagtgat 2460
gtatggagct atggaatcgt tatgtgggaa gtgatgtcgt acggggagag gccctattgg 2520
gatatgtcca atcaagatgt gattaaagcc attgaggaag gctatcggtt acccctcca 2580
atggactgcc ccattgcgct ccaccagctg atgctagact gctggcagaa ggagaggagc 2640
gacaggccta aatttgggca gattgtcaac atgttggaca aactcatccg caaccccaac 2700
agcttgaaga ggacagggac ggagagctcc agacctaaca ctgccttgtt ggatccaagc 2760
tcccctgaat tctctgctgt ggtatcagtg ggcgattggc tccaggccat taaaatggac 2820
cggtataagg ataacttcac agctgctggt tataccacac tagaggctgt ggtgcacgtg 2880
aaccaggagg acctggcaag aattggtatc acagccatca cgcaccagaa taagattttg 2940
agcagtgtcc aggcaatgcg aacccaaatg cagcagatgc acggcagaat ggttcccgtc 3000
tgagccagta ctgaataaac tcaaaactct tgaaattagt ttacctcatc catgcacttt 3060
aattgaagaa ctgcactttt tttacttcgt cttcgccctc tgaaattaaa gaaatgaaaa 3120
aaaaaaacaa tatctgcagc gttgcttggt gcacagattg ctgaaactgt ggggcttaca 3180
gaaatgactg ccggtcattt gaatgagacc tggaacaaat cgtttctcag aagtactttt 3240
ctgttcatca ccagtctgta aaatacatgt acctatagaa atagaacact gcctctgagt 3300
tttgatgctg tatttgctgc cagacactga gcttctgaga catccctgat tctctctcca 3360
tttggaatta caaccattgt attttgtttg tggcataaat tacagtcatc tgtctttcac 3420
tggaatgaag accatgccta ggaacatttt ttaaggactc agctgtggct tttagggctt 3480
ggttcatacc atgggggaaa aaaaagtcct aggagaaagc gacgtggctc attagtgttg 3540
cctcttcagt gctcaagccg cctggtggat tcctatgaca caggggcct ggaaagaaag 3600
ggaaagtgga tttaaaatat atatatacgt aacccaagcc ccataacccc taactggaca 3660
aatgaggtct gtttctttgg gcctgaggct gtgccatata aagtcttatt ttgggacttt 3720
acaaacttgt cctaactatc ttgtggatag tgggctgtga caatctggaa tagagaacgt 3780
tcacacttcg ctcctttaaa gaagcgaccc cagatctgca agggagtaga ttctgctatc 3840

ttggcctcac agcccttcct gttgattaca aagcccgtgg aagaaaacag aacacaccct 3900
cctcagttcc gtctaaatgt gtttcttctg cttcaattac accagttctg gggcaaagac 3960
actgatgaaa caacacccat acctgaaaag aataaatgtg tgactttcaa atccccttc 4020
gcagtgaaag aaacagcaaa cacttaagat tcagcatctg ttctccagtt gcactgagga 4080
atgcactgtc tcgcagcacc agctctgcag agcccttgcc ccagactctt tgcggtttta 4140
tttatatgta tttccatatt tcattcctgt gtgtcactgc tgcattggtg tggcagcaag 4200
tgaccaaatg ctacaggtct tactatggac accaggtcag gtgcaaccac acaaaacaaa 4260
gccagttcca tgagctgcct atgatatgca ttgcggaagt aacattttac ccagggtgtg 4320
ccattgcagt gatataaata tatttttttc ttagactaaa tatgagctga ctatctcttt 4380
tgatgtgtgt acataggtgt gagtgtgtgt gtatgcgtgc ctgtctgtgt gcgggtgtgt 4440
gtatgtgcat agcctcatgc ttaggactac ccatgaatgt tgtggaatgc tacacctgga 4500
gagttctggt tttccaccag tttcaagatg aagaactaca tgatacagtg gacctggaga 4560
ccatcccctt ggaaagacaa cccagagatg ttcagcatcc tgtatctaca cgcatcctgt 4620
atctacacgt gtattttgta gctgtcacac taaccttaat aagaattcta cagctttgga 4680
cagaggcatt ttcaccttaa tggtgaagta atttaaaata taaatccatt caggtgacaa 4740
cccatcatca aaattacaaa ttttctgatt gaactcatct gaatcatcag ttccttgatg 4800
gagagagaga aggagatgga atgtgtctgg taaccccaaa tggagtacaa gtagcctttg 4860
ttttcctgca taaatggact tgttgaatgc gaacgaatat atgcaattca tatacttttg 4920
gagatgaacg tagatatgtg tgtcagcttt gagatggtgt gtcctggatt aatacttttgt 4980
ctcccaatat cacagaaaaa tacatgccag tgactcttga ggttaaggta gttgggatga 5040
aatggcctca ggcaatttca cattccctaa ttacctggaa agttctacag taattaatat 5100
gcagctaact cctgttgccc tcacaagagc atcagccttc tagaatcgga gctccggagt 5160
gtgaagattc agtattgata tgatatgtat accaaactcc agccaactta ctgccatttt 5220
tcataatctg agtggctgcc ttgcttatcc taagctgtgg ttgcagaaac cgtggccatt 5280
tatataagct ataacatcaa atcagggaaa aatgaggaaa aaaaatagat tctgaaccat 5340
ttattgttga ataagtagag aaaatcatca ataaatattt attacattct gacagggtgt 5400
gtggcattgt gttctatgcc agagtgacaa agttgattca ccccttttg gggaccttaa 5460
tatatttttt aagggatgtg cctatgcatt gatgcctgaa aaatatgtat aaagaaatga 5520
ggttgactct tctgagcagt tcatcttttc cagaggtaag ggtaggaggc caacttcagg 5580
gtctgggtct gagcccgtgg gcaagccctg gccgagtgag ctccaatgct aactcatgtg 5640
ccgatctcta gagcagtggg aaactacccc gctgcaccaa atcaagtagc ttcaccttgt 5700
gtatgcaggc cccaagttat tttttagcaa tcttacgagt gaaatgttct ggtgggttga 5760
aaaacgttct tattttaaag aaaggttgtg ctcgctacac tgctggtgtg tgcattctga 5820
gacctcttgt attcaatctg tgaaggatat gtgtattaat ccgtacaccc gtatagcctc 5880
aatatttgtc tgaagacact taaattctga cccataaagg aaagttctag aagcaatatt 5940
ttcacttatt taacattctc caaacaacat caagcattga tacacactga agagtgcgtt 6000
tatttttgt atcactctaa gtatgttgga atatgcaagg actgtggttc aaattagaat 6060
gtataaggca tattataatt tagttcatac tgaataagaa attaacagaa cattgttcgg 6120
ttcacacgtt ccaaactttg agtgatttct ggagttagac atagattttc tattttgttt 6180
taatttgtca aggtatttttt cttcccttca tgaactttag gtacacataa cttatgtcat 6240
ttatttatgg tcttttatac ctagtttgta aaattgtaaa atagcaaact aaatgcaaag 6300
agtttgcatt tgaaaataat aaagtagttg ccgtatacaa ccctgcaaaa aaaaaaaaaa 6360
aaaa 6364

<210> 232
<211> 3162
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. L36644
<309> 1995-08-10

<400> 232

ccagcgtccc tggccggctg ctactctgca cctcgacggg ctcccctctg gacgtgcctt 60
ctcctgtgcg ccgcactccg gaccctcctg gccagcccca gcaacgaagt gaatttattg 120
gattcacgca ctgtcatggg ggacctggga tggattgctt ttccaaaaaa tgggtgggaa 180
gagattggtg aagtggatga aaattatgcc cctatccaca cataccaagt atgcaaagtg 240
atggaacaga atcagaataa ctggcttttg accagttgga tctccaatga aggtgcttcc 300
agaatcttca tagaactcaa atttaccctg cgggactgca acagccttcc tggaggactg 360
gggacctgta aggaaacctt taatatgtat tactttgagt cagatgatca gaatgggaga 420
aacatcaagg aaaaccaata catcaaaatt gataccattg ctgccgatga aagctttaca 480
gaacttgatc ttggtgaccg tgttatgaaa ctgaatacag aggtcagaga tgtaggacct 540
ctaagcaaaa agggatttta tcttgctttt caagatgttg gtgcttgcat tgctctggtt 600
tctgtgcgtg tatactataa aaaatgccct tctgtggtac gacacttggc tgtcttccct 660
gacaccatca ctggagctga ttcttcccaa ttgctcgaag tgtcaggctc ctgtgtcaac 720
cattctgtga ccgatgaacc tcccaaaatg cactgcagcg ccgaagggga gtggctggtg 780
cccatcggga aatgcatgtg caaggcagga tatgaagaga aaaatggcac ctgtcaagtg 840
tgcagacctg ggttcttcaa agcctcacct cacatccaga gctgcggcaa atgtccacct 900
cacagttata cccatgagga agcttcaacc tcttgtgtct gtgaaaagga ttatttcagg 960
agagagtctg atccacccac aatggcatgc acaagacccc cctctgctcc tcggaatgcc 1020
atctcaaatg ttaatgaaac tagtgtcttt ctggaatgga ttccgcctgc tgacactggt 1080
ggaaggaaag acgtgtcata ttatattgca tgcaagaagt gcaactccca tgcaggtgtg 1140
tgtgaggagt gtggcggtca tgtcaggtac cttccccggc aaagcggcct gaaaaacacc 1200
tctgtcatga tggtggatct actcgctcac acaaactata cctttgagat tgaggcagtg 1260
aatggagtgt ccgacttgag cccaggagcc cggcagtatg tgtctgtaaa tgtaaccaca 1320
aatcaagcag ctccatctcc agtcaccaat gtgaaaaaag ggaaaattgc aaaaaacagc 1380
atctctttgt cttggcaaga accagatcgt cccaatggaa tcatcctaga gtatgaaatc 1440
aagcattttg aaaaggacca agagaccagc tacacgatta tcaaatctaa agagacaact 1500
attactgcag agggcttgaa accagcttca gtttatgtct tccaaattcg agcacgtaca 1560
gcagcaggct atggtgtctt cagtcgaaga tttgagtttg aaaccacccc agtgtttgca 1620
gcatccagcg atcaaagcca gattcctgta attgctgtgt ctgtgacagt aggagtcatt 1680
ttgttggcag tggttatcgg cgtcctcctc agtggaaggc ggtgtggcta cagcaaagca 1740
aaacaagatc cagaagagga aaagatgcat tttcataatg ggcacattaa actgccagga 1800
gtaagaactt acattgatcc acatacctat gaggatccca atcaagctgt ccacgaattt 1860
gccaaggaga tagaagcatc atgtatcacc attgagagag ttattggagc aggtgaattt 1920
ggtgaagttt gtagtggacg tttgaaacta ccaggaaaaa gagaattacc tgtggctatc 1980
aaaaccctta aagtaggcta tactgaaaag caacgcagag atttcctagg tgaagcaagt 2040
atcatgggac agtttgatca tcctaacatc atccatttag aaggtgtggt gaccaaaagt 2100
aaaccagtga tgatcgtgac agagtatatg gagaatggct ctttagatac atttttgaag 2160
aaaaacgatg ggcagttcac tgtgattcag cttgttggca tgctgagagg tatctctgca 2220
ggaatgaagt acctttctga catgggctat gtgcatagag atcttgctgc cagaaacatc 2280
ttaatcaaca gtaaccttgt gtgcaaagtg tctgactttg gactttcccg ggtactggaa 2340
gatgatcccg aggcagccta caccacaagg ggaggaaaaa ttccaatcag atggactgcc 2400
ccagaagcaa tagctttccg aaagtttact tctgccagtg atgtctggag ttatggaata 2460
gtaatgtggg aagttgtgtc ttatggagag agaccctact gggagatgac caatcaagat 2520
gtgattaaag cggtagagga aggctatcgt ctgccaagcc ccatggattg tcctgctgct 2580
ctctatcagt taatgctgga ttgctggcag aaagagcgaa atagcaggcc caagtttgat 2640
gaaatagtca acatgttgga caagctgata cgtaacccaa gtagtctgaa gacgctggtt 2700
aatgcatcct gcagagtatc taatttattg gcagaacata gcccactagg atctggggcc 2760
tacagatcag taggtgaatg gctagaggca atcaagatgg gccggtatac agagattttc 2820
atggaaaatg gatacagttc aatggacgct gtggctcagg tgaccttgga ggatttgaga 2880
cggcttggag tgactcttgt cggtcaccag aagaagatca tgaacagcct tcaagaaatg 2940
aaggtgcagc tggtaaacgg aatggtgcca ttgtaacttc atgtaaatgt cgcttcttca 3000
agtgaatgat tctgcacttt gtaaacagca ctgagattta ttttaacaaa aaaaggggga 3060
aaagggaaaa cagtgatttc taaaccttag aaaacatttg cctcagccac agaatttgta 3120
atcatggttt tactgaagta tccagttctt agtccttagt ct 3162

<210> 233
<211> 1619

<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. AL133666
<309> 2005-01-20

<400> 233
aggaaagcta agacaaacaa aactacaatg gaagaagaaa acgtcctcaa ctagacatct 60
gccaaaaata tcatccagaa tgccctggca agttcacttc catttagtga agtgagataa 120
tttggcaatt cacgcaagag actgagaacc aagcctcaag ccctgcctct gattctgcag 180
gtatggaaca tgagcagctg acctactctt ccacaaggtc caaagccccc agtgtcatca 240
tcacaggtct taagccagcc accaaatatg tatttcacat ccgagtgaga actgcgacag 300
gatacagtgg ctacagtcag aaatttgaat ttgaaacagg agatgaaaga ctctccattt 360
caagtgacaa aactgtactg gcttaatgaa aagtgggact ttattgcctc agcttctgac 420
atggcagcag aacaaggaca gattctcgtg atagccaccg ccgctgttgg cggattcact 480
ctcctcgtca tcctcacttt attcttcttg atcactggga gatgtcagtg gtacataaaa 540
gccaagatga agtcagaaga gaagagaaga aaccacttac agaatgggca tttgcgcttc 600
ccgggaatta aaacttacat tgatccagat acatatgaag acccatccct agcagtccat 660
gaatttgcaa aggagattga tccctcaaga attcgtattg agagagtcat tggggcaggt 720
gaatttggag aagtctgtag tgggcgtttg aagacaccag ggaaaagaga gatcccagtt 780
gccattaaaa ctttgaaagg tggccacatg gatcggcaaa gaagagattt tctaagagaa 840
gctagtatca tgggccagtt tgaccatcca aacatcattc gcctagaagg ggttgtcacc 900
aaaagatcct tcccggccat tggggtggag gcgttttgcc ccagcttcct gagggcaggg 960
tttttaaata gcatccaggc cccgcatcca gtgccagggg gaggatcttt gccccccagg 1020
attcctgctg gcagaccagt aatgattgtg gtggaatata tggagaatgg atccctagac 1080
tccttttgc ggaagcatga tggccacttc acagtcatcc agttggtcgg aatgctccga 1140
ggcattgcat caggcatgaa gtatctttct gatatgggtt atgttcatcg agacctagcg 1200
gctcggaata tactggtcaa tagcaactta gtatgcaaag tttctgattt tggtctctcc 1260
agagtgctgg aagatgatcc agaagctgct tatacaacaa ctgacctctt ccaaactcta 1320
acacttaacc tctgctattc tgcataaatt ctgagaaaag ccaaattttc tgtcggtcta 1380
agaagacata gcctacaccc aactggagat aattataaaa aataatgaag cagcatgagg 1440
ggaaggtatt taatgtgtat tttaaagttg ggagagattc tccttcacct aatttaggtg 1500
tttgtgaatt ggcttgactt tttgaagtta atttttaagc cttgaacatg tccaacttta 1560
agaactttaa gaataaatat tttaacacaa gtgaaaaaaa aaaaaaaaaa aaaaaaagg 1619

<210> 234
<211> 4996
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004440
<309> 2005-01-26

<400> 234
gcgccggggt gtgcgcccgg ccgggtgtgc ggagagcgag ggagcgcgct ccctcccgac 60
gcgcgggccg cagcggccaa gcccgagggt gcgtggcgcc cccgcccgcc cggcccggcc 120
cggccatggc ccccgcccgg ggccgcctgc cccctgcgct ctgggtcgtc acggccgcgg 180
cggcggcggc cacctgcgtg tccgcggcgc gcggcgaagt gaatttgctg gacacgtcga 240
ccatccacgg ggactggggc tggctcacgt atccggctca tgggtgggac tccatcaacg 300
aggtggacga gtccttccag cccatccaca cgtaccaggt ttgcaacgtc atgagcccca 360
accagaacaa ctggctgcgc acgagctggg tcccccgaga cggcgcccgg cgcgtctatg 420
ctgagatcaa gtttaccctg cgcgactgca acagcatgcc tggtgtgctg ggcacctgca 480
aggagacctt caacctctac tacctggagt cggaccgcga cctgggggcc agcacacaag 540
aaagccagtt cctcaaaatc gacaccattg cggccgacga gagcttcaca ggtgccgacc 600

ttggtgtgcg gcgtctcaag ctcaacacgg aggtgcgcag tgtgggtccc ctcagcaagc 660
gcggcttcta cctggccttc caggacatag gtgcctgcct ggccatcctc tctctccgca 720
tctactataa gaagtgccct gccatggtgc gcaatctggc tgccttctcg gaggcagtga 780
cgggggccga ctcgtcctca ctggtggagg tgaggggcca gtgcgtgcgg cactcagagg 840
agcgggacac acccaagatg tactgcagcg cggagggcga gtggctcgtg cccatcggca 900
aatgcgtgtg cagtgccggc tacgaggagc ggcgggatgc ctgtgtggcc tgtgagctgg 960
gcttctacaa gtcagcccct ggggaccagc tgtgtgcccg ctgccctccc cacagccact 1020
ccgcagctcc agccgcccaa gcctgccact gtgacctcag ctactaccgt gcagccctgg 1080
acccgccgtc ctcagcctgc acccggccac cctcggcacc agtgaacctg atctccagtg 1140
tgaatgggac atcagtgact ctggagtggg cccctcccct ggacccaggt ggccgcagtg 1200
acatcaccta caatgccgtg tgccgccgct gcccctgggc actgagccgc tgcgaggcat 1260
gtgggagcgg cacccgcttt gtgccccagc agacaagcct ggtgcaggcc agcctgctgg 1320
tggccaacct gctggcccac atgaactact ccttctggat cgaggccgtc aatggcgtgt 1380
ccgacctgag ccccgagccc cgccgggccg ctgtggtcaa catcaccacg aaccaggcag 1440
ccccgtccca ggtggtggtg atccgtcaag agcgggcggg gcagaccagc gtctcgctgc 1500
tgtggcagga gcccgagcag ccgaacggca tcatcctgga gtatgagatc aagtactacg 1560
agaaggacaa ggagatgcag agctactcca ccctcaaggc cgtcaccacc agagccaccg 1620
tctccggcct caagccgggc acccgctacg tgttccaggt ccgagcccgc acctcagcag 1680
gctgtggccg cttcagccag gccatggagg tggagaccgg gaaaccccgg ccccgctatg 1740
acaccaggac cattgtctgg atctgcctga cgctcatcac gggcctggtg gtgcttctgc 1800
tcctgctcat ctgcaagaag aggcactgtg gctacagcaa ggccttccag gactcggacg 1860
aggagaagat gcactatcag aatggacagg cacccccacc tgtcttcctg cctctgcatc 1920
acccccgggg aaagctccca gagccccagt tctatgcgga accccacacc tacgaggagc 1980
caggccgggc gggccgcagt ttcactcggg agatcgaggc ctctaggatc cacatcgaga 2040
aaatcatcgg ctctggagac tccggggaag tctgctacgg gaggctgcgg gtgccagggc 2100
agcgggatgt gcccgtggcc atcaaggccc tcaaagccgg ctacacggag agacagaggc 2160
gggacttcct gagcgaggcg tccatcatgg ggcaattcga ccatcccaac atcatccgcc 2220
tcgagggtgt cgtcacccgt ggccgcctgg caatgattgt gactgagtac atggagaacg 2280
gctctctgga caccttcctg aggacccacg acgggcagtt caccatcatg cagctggtgg 2340
gcatgctgag aggagtgggt gccggcatgc gctacctctc agacctgggc tatgtccacc 2400
gagacctggc cgcccgcaac gtcctggttg acagcaacct ggtctgcaag gtgtctgact 2460
tcgggctctc acgggtgctg gaggacgacc cggatgctgc ctacaccacc acgggcggga 2520
agatccccat ccgctggacg gccccagagg ccatcgcctt ccgcaccttc tcctcggcca 2580
gcgacgtgtg gagcttcggc gtggtcatgt gggaggtgct ggcctatggg gagcggccct 2640
actggaacat gaccaaccgg gatgtcatca gctctgtgga ggaggggtac cgcctgcccg 2700
cacccatggg ctgcccccac gccctgcacc agctcatgct cgactgttgg cacaaggacc 2760
gggcgcagcg gcctcgcttc tcccagattg tcagtgtcct cgatgcgctc atccgcagcc 2820
ctgagagtct cagggccacc gccacagtca gcaggtgccc acccctgcc ttcgtccgga 2880
gctgctttga cctccgaggg ggcagcggtg gcggtggggg cctcaccgtg ggggactggc 2940
tggactccat ccgcatgggc cggtaccgag accacttcgc tgcgggcgga tactcctctc 3000
tgggcatggt gctacgcatg aacgcccagg acgtgcgcgc cctgggcatc accctcatgg 3060
gccaccagaa gaagatcctg ggcagcattc agaccatgcg ggcccagctg accagcaccc 3120
aggggccccg ccggcacctc tgatgtacag ccagcagggc ccaggcagcc accaagccca 3180
ccccaggtca tgccagcggc agaggacgtg aggggctggc agcaggcagg gcggccccag 3240
gcctctgccc tcctctcagg tgctggagga gctgaaggct tcgccacagg acctggagtt 3300
atcaggggtc aggcgcctgg gaaggggcct ttggtggcca ccctggtgag gacacctgtc 3360
ccccagggca ggcaccttct cttttccaga gcctggggcc tccacgtcac agagtccaac 3420
agggacatca ctcgcctgcc tctgtgtgcg tgcatgtgtg tgtgtggtgg ggggtgttct 3480
cacaaggtca tgggatctca tgtgaacagt gtgtgatcaa gtgtgtccac cccttcgggt 3540
ctcagcatgg acgtgtgcat gttatgagcg tgtgcttatc cgttaaggct ggaggcacat 3600
gtgggtgatg gtggatgatg tgtcatgaat gaggaggtgt gtgagcaggg aactcagtgt 3660
gacaccgcca ggtccagcac ccatgggggc gggggagagg ctcaccccta cgtcccccca 3720
cacctggagg ctggagccag gggccacttc tgaactgcac cagcaccagg cccaccctcg 3780
tctctgcctg ggtgagccca ccccggctgt atctcaggtc tgggtcctcc ctctagccga 3840
ggaggccacc tgcagcctcc acccggctct caccgctgct tcaacaggaa aacagggttc 3900
ccggtcagtc cggctggccg ccttcatgga ggcatcatgg cagagcacat gagatgtcct 3960

cagctgggct tggctgcctg gccagggccg ggggctcagc agcctcctct agcctctgat 4020
gccttccctc cacggcccag gtctcctcac tcaaagtccc ttcgccaacc tttcaatgcc 4080
cagccctgac acctgcccтt tgtcccccag gcctaggatc agggaccaga ggatcctatc 4140
ttctcagcac ccagcccacc ccttcctgta gcatatgggg agactaaggc ctggagagag 4200
gggtgatgcc ccgtcccagg ttgcactgca accaagtgtc agagtcgggg ctccggcctc 4260
ctgccaaggc tcttgtcccc atacaccatc ccacaagggc gctgggggtg gaagtgccct 4320
ggaagcccct ccctctcac actgacctcc ccccttacgg cccaccaggg tatgtaaata 4380
tctcttttct accatgtcag aatatttttt cctcactcct gacaatgcaa aaatggtctt 4440
caaagcacat aaaaagcacc cagggtgaga aagccccatc ccgggggccg ttggcaggca 4500
gggaagcagg aaccccaccg tgtgcccccт gccagcccca gagggagtgg cgagcccagc 4560
tgcccagccc tgcccccccт ccccatagcc agcacagcta tcccgcgggg acaccagcac 4620
tgagcccccт ctccctcctg caataattcg gggagtctca gccccatcca ggtgccgcgg 4680
ccagctctct acacctctat atattatatt actatatagc cgagctgttc ttccttccta 4740
tggaagtcgg aaacatggtc agaacacgat ctgggggggg gatcctgtct tcctccccac 4800
cccaccccac tcttacccaa tttctgggct ctggatcctc acagtcatgg aggcaccgtg 4860
ggcctggcac ttgcaaaagt gtggcccctc actctagtgt gtggtccctc tcagggtcct 4920
ggggatctgc ctctctgtgg tctccatcct gactcttgaa cttacccaca ataagaataa 4980
attctgcctc atcttt 4996

<210> 235
<211> 5229
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM020526
<309> 2004-11-16

<400> 235
gcagtcggag acttgcaggc agcaaacacg gtgcgagcga acaggagtgg gggggaaatt 60
aaaaaaagct aaacgtggag cagccgatcg gggaccgaga aggggaatcg atgcaaggag 120
cacaataaaa caaaagctac ttcggaacaa acagcattta aaaatccacg actcaagata 180
actgaaacct aaaataaaac ctgctcatgc accatggttt ttcaaactcg gtacccttca 240
tggattattt tatgctacat ctggctgctc cgctttgcac acacagggga ggcgcaggct 300
gcgaaggaag tactactgct ggattctaaa gcacaacaaa cagagttgga gtggatttcc 360
tctccaccca atgggtggga agaaattagt ggtttggatg agaactatac cccgatacga 420
acataccagg tgtgccaagt catggagccc aaccaaaaca actggctgcg gactaactgg 480
atttccaaag gcaatgcaca aaggattttt gtagaattga aattcaccct gagggattgt 540
aacagtcttc ctggagtact gggaacttgc aaggaaacat ttaatttgta ctattatgaa 600
acagactatg acactggcag gaatataaga gaaaacctct atgtaaaaat agacaccatt 660
gctgcagatg aaagttttac ccaaggtgac cttggtgaaa gaaagatgaa gcttaacact 720
gaggtgagag agattggacc tttgtccaaa aagggattct atcttgcctt tcaggatgta 780
ggggcttgca tagctttggt ttctgtcaaa gtgtactaca agaagtgctg gtccattatt 840
gagaacttag ctatctttcc agatacagtg actggttcag aattttcctc tttagtcgag 900
gttcgaggga catgtgtcag cagtgcagag gaagaagcgg aaaacgcccc caggatgcac 960
tgcagtgcag aaggagaatg gttagtgccc attggaaaat gtatctgcaa agcaggctac 1020
cagcaaaaag gagacacttg tgaaccctgt ggccgtgggt tctacaagtc ttcctctcaa 1080
gatcttcagt gctctcgttg tccaactcac agtttttctg ataaagaagg ctcctccaga 1140
tgtgaatgtg aagatgggta ttacagggct ccatctgacc caccatacgt tgcatgcaca 1200
aggcctccat ctgcaccaca gaacctcatt ttcaacatca accaaaccac agtaagtttg 1260
gaatggagtc ctcctgcaga caatggggga agaaacgatg tgacctacag aatattgtgt 1320
aagcggtgca gttgggagca gggcgaatgt gttccctgtg ggagtaacat tggatacatg 1380
ccccagcaga ctggattaga ggataactat gtcactgtca tggacctgct agcccacgct 1440
aattatactt ttgaagttga agctgtaaat ggagtttctg acttaagccg atcccagagg 1500
ctctttgctg ctgtcagtat caccactggt caagcagctc cctcgcaagt gagcggagta 1560
atgaaggaga gagtactgca gcggagtgtc gagctttcct ggcaggaacc agagcatccc 1620

aatggagtca tcacagaata tgaaatcaag tattacgaga aagatcaaag ggaacggacc 1680
tactcaacag taaaaaccaa gtctacttca gcctccatta ataatctgaa accaggaaca 1740
gtgtatgttt tccagattcg ggcttttact gctgctggtt atggaaatta cagtcccaga 1800
cttgatgttg ctacactaga ggaagctaca ggtaaaatgt ttgaagctac agctgtctcc 1860
agtgaacaga atcctgttat tatcattgct gtggttgctg tagctgggac catcattttg 1920
gtgttcatgg tctttggctt catcattggg agaaggcact gtggttatag caaagctgac 1980
caagaaggcg atgaagagct ttactttcat tttaaatttc caggcaccaa aacctacatt 2040
gaccctgaaa cctatgagga cccaaataga gctgtccatc aattcgccaa ggagctagat 2100
gcctcctgta ttaaaattga gcgtgtgatt ggtgcaggag aattcggtga agtctgcagt 2160
ggccgtttga aacttccagg gaaaagagat gttgcagtag ccataaaaac cctgaaagtt 2220
ggttacacag aaaaacaaag gagagacttt ttgtgtgaag caagcatcat ggggcagttt 2280
gaccacccaa atgttgtcca tttggaaggg gttgttacaa gagggaaacc agtcatgata 2340
gtaatagagt tcatggaaaa tggagcccta gatgcatttc tcaggaaaca tgatgggcaa 2400
tttacagtca ttcagttagt aggaatgctg agaggaattg ctgctggaat gagatatttg 2460
gctgatatgg gatatgttca cagggacctt gcagctcgca atattcttgt caacagcaat 2520
ctcgtttgta aagtgtcaga ttttggcctg tcccgagtta tagaggatga tccagaagct 2580
gtctatacaa ctactggtgg aaaaattcca gtaaggtgga cagcacccga agccatccag 2640
taccggaaat tcacatcagc cagtgatgta tggagctatg gaatagtcat gtgggaagtt 2700
atgtcttatg gagaaagacc ttattgggac atgtcaaatc aagatgttat aaaagcaata 2760
gaagaaggtt atcgtttacc agcacccatg gactgcccag ctggccttca ccagctaatg 2820
ttggattgtt ggcaaaagga gcgtgctgaa aggccaaaat ttgaacagat agttggaatt 2880
ctagacaaaa tgattcgaaa cccaaatagt ctgaaaactc ccctgggaac ttgtagtagg 2940
ccaataagcc ctcttctgga tcaaaacact cctgatttca ctacctttg ttcagttgga 3000
gaatggctac aagctattaa gatggaaaga tataaagata atttcacggc agctggctac 3060
aattcccttg aatcagtagc caggatgact attgaggatg tgatgagttt agggatcaca 3120
ctggttggtc atcaaaagaa aatcatgagc agcattcaga ctatgagagc acaaatgcta 3180
catttacatg gaactggcat tcaagtgtga tatgcatttc tccctttaa gggagattac 3240
agactgcaag agaacagtac tggccttcag tatatgcata gaatgctgct agaagacaag 3300
tgatgtcctg ggtccttcca acagtgaaga gaagatttaa gaagcaccta tagacttgaa 3360
ctcctaagtg ccaccagaat atataaaaag ggaatttagg atccaccatc ggtggccagg 3420
aaaatagcag tgacaataaa caaagtacta cctgaaaaac atccaaacac cttgagctct 3480
ctaacctcct ttttgtctta tagacttttt aaaatgtaca taaagaattt aagaaagaat 3540
atatttgtca aataaaatca tgatcttatt gttaaaatta atgaaatatt ttccttaaat 3600
atgtgatttc agactattcc tttttaaaat catttgtgtt tattcttcat aaggactttg 3660
ttttagaaag ctgtttatag ctttggacct ttttagtgtt aaatctgtaa cattactaca 3720
ctgggtacct ttgaaagaat ctcaaatttc aaaagaaata gcatgattga agatacatct 3780
ctgttagaac attggtatcc tttttgtgcc attttattct gtttaatcag tgctgttttg 3840
atattgtttg ctaattggca ggtagtcaag aaaatgcaag ttgccaagag ctctgatatt 3900
ttttaaaaag aatttttttg taaagatcag acaacacact atcttttcaa tgaaaaaagc 3960
aataatgatc catacatact ataaggcact tttaacagat tgtttataga gtgattttac 4020
tagaaagaat ttaataaact cgaagtttag gtttatgagt atataaacaa atgaggcact 4080
tcatctgaag aatgttggtg aaggcaagtc tctgaaagca gaactatcca gtgttatcta 4140
aaaattaatc tgagcacatc aagatttttt cattctcgtg acattaggaa atttaggata 4200
aatagttgac atatatttta tatcctcttc tgttgaatgc agtccaaaca tgaaaggaaa 4260
taattgtttt atattataac tctgaagcat gataaagggg cagttcacaa ttttcaccat 4320
ttaaacacaa atttgctgca cagaatatca ccattgcagt tcaaaacaaa acaaaacaaa 4380
aagtcttttg tttgtgaaca ctgatgcaag aaacttgtta aatgaaagga ctctttaccc 4440
tagaaggaag aggtgaagga tctggcttgt ttttaaagct ttatttatta aaccatatta 4500
tttgattact gtgttagaat ttcataagca ataattaaat gtgtctttat agatattgca 4560
ggaatgtata catattgtga ttaatgcttt caaaacttat gaaaatcatg aactacccca 4620
gaattgaact gttgtacttc caaagagaat tgggctgttt ataatgattt taatagagaa 4680
agatcccagg gatcggtcat aattggtctt gtttgataat gtgggcatcc acaaacaaac 4740
aaacaaataa cagaaacaaa atctgtaaat gttcctttgt aaaacttgta aattttattt 4800
atactgtctt gttttgtaca cacatttctc tgtagtgggc tctgaataca ttgaaaatgc 4860
actatatttt tctattttac ttgcagagca tcacaaaaga acaggtattt tcagtgctac 4920
ataatgtgtt ttcccacatt taggaccaaa gacggctata gaaaaactca aatggattgc 4980

ttcccaaacc cctccccacc ctttttttt ggttttaaat cactgtacag tgttatttga 5040
tattttaatt tatttttga ttgactagaa aaatcatttt aatttcacta aaatgttttt 5100
tgtccctaag gaaaagtaat ctgtaaaaat aattttaatt agcataatac agtcacctag 5160
acacttccat ttgtaatctt tgtaatagac tgtaaatata tttttggaac tataaaaaaa 5220
aaaaaaaaa 5229

<210> 236
<211> 3949
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. AF025304
<309> 2000-11-29

<400> 236
gaattccgcc ccgggaagcg cagccatggc tctgcggagg ctgggggccg cgctgctgct 60
gctgccgctg ctcgccgccg tggaagaaac gctaatggac tccactacag cgactgctga 120
gctgggctgg atggtgcatc ctccatcagg gtgggaagag gtgagtggct acgatgagaa 180
catgaacacg atccgcacgt accaggtgtg caacgtgttt gagtcaagcc agaacaactg 240
gctacggacc aagtttatcc ggcgccgtgg cgcccaccgc atccacgtgg agatgaagtt 300
ttcggtgcgt gactgcagca gcatccccag cgtgcctggc tcctgcaagg agaccttcaa 360
cctctattac tatgaggctg actttgactc ggccaccaag accttcccca actggatgga 420
gaatccatgg gtgaaggtgg ataccattgc agccgacgag agcttctccc aggtggacct 480
gggtggccgc gtcatgaaaa tcaacaccga ggtgcggagc ttcggacctg tgtcccgcag 540
cggcttctac ctggccttcc aggactatgg cggctgcatg tccctcatcg ccgtgcgtgt 600
cttctaccgc aagtgccccc gcatcatcca gaatggcgcc atcttccagg aaaccctgtc 660
gggggctgag agcacatcgc tggtggctgc ccggggcagc tgcatcgcca atgcggaaga 720
ggtggatgta cccatcaagc tctactgtaa cggggacggc gagtggctgg tgcccatcgg 780
gcgctgcatg tgcaaagcag gcttcgaggc cgttgagaat ggcaccgtct gccgaggttg 840
tccatctggg actttcaagg ccaaccaagg ggatgaggcc tgtacccact gtcccatcaa 900
cagccggacc acttctgaag gggccaccaa ctgtgtctgc cgcaatggct actacagagc 960
agacctggac cccctggaca tgccctgcac aaccatcccc tccgcgcccc aggctgtgat 1020
ttccagtgtc aatgagacct ccctcatgct ggagtggacc cctccccgcg actccggagg 1080
ccgagaggac ctcgtctaca acatcatctg caagagctgt ggctcgggcc ggggtgcctg 1140
cacccgctgc ggggacaatg tacagtacgc accacgccag ctaggcctga ccgagccacg 1200
catttacatc agtgacctgc tggcccacac ccagtacacc ttcgagatcc aggctgtgaa 1260
cggcgttact gaccagagcc ccttctcgcc tcagttcgcc tctgtgaaca tcaccaccaa 1320
ccaggcagct ccatcggcag tgtccatcat gcatcaggtg agccgcaccg tggacagcat 1380
taccctgtcg tggtcccagc cagaccagcc caatggcgtg atcctggact atgagctgca 1440
gtactatgag aaggagctca gtgagtacaa cgccacagcc ataaaaagcc ccaccaacac 1500
ggtcaccgtg cagggcctca aagccggcgc catctatgtc ttccaggtgc gggcacgcac 1560
cgtggcaggc tacgggcgct acagcggcaa gatgtacttc cagaccatga cagaagccga 1620
gtaccagaca agcatccagg agaagttgcc actcatcatc ggctcctcgg ccgctggcct 1680
ggtcttcctc attgctgtgg ttgtcatcgc catcgtgtgt aacagacggg ggtttgagcg 1740
tgctgactcg gagtacacgg acaagctgca acactacacc agtggccaca tgaccccagg 1800
catgaagatc tacatcgatc ctttcaccta cgaggacccc aacgaggcag tgcgggagtt 1860
tgccaaggaa attgacatct cctgtgtcaa aattgagcag gtgatcggag caggggagtt 1920
tggcgaggtc tgcagtggcc acctgaagct gccaggcaag agagagatct ttgtggccat 1980
caagacgctc aagtcgggct acacggagaa gcagcgccgg gacttcctga gcgaagcctc 2040
catcatgggc cagttcgacc atcccaacgt catccacctg gagggtgtcg tgaccaagag 2100
cacacctgtg atgatcatca ccgagttcat ggagaatggc tccctggact cctttctccg 2160
gcaaaacgat gggcagttca cagtcatcca gctggtgggc atgcttcggg gcatcgcagc 2220
tggcatgaag tacctggcag acatgaacta tgttcaccgt gacctggctg cccgcaacat 2280

cctcgtcaac agcaacctgg tctgcaaggt gtcggacttt gggctctcac gctttctaga 2340
ggacgatacc tcagacccca cctacaccag tgccctgggc ggaaagatcc ccatccgctg 2400
gacagccccg gaagccatcc agtaccggaa gttcacctcg gccagtgatg tgtggagcta 2460
cggcattgtc atgtgggagg tgatgtccta tggggagcgg ccctactggg acatgaccaa 2520
ccaggatgta atcaatgcca ttgagcagga ctatcggctg ccaccgccca tggactgccc 2580
gagcgccctg caccaactca tgctggactg ttggcagaag gaccgcaacc accggcccaa 2640
gttcggccaa attgtcaaca cgctagacaa gatgatccgc aatcccaaca gcctcaaagc 2700
catggcgccc ctctcctctg gcatcaacct gccgctgctg gaccgcacga tccccgacta 2760
caccagcttt aacacggtgg acgagtggct ggaggccatc aagatggggc agtacaagga 2820
gagcttcgcc aatgccggct tcacctcctt tgacgtcgtg tctcagatga tgatggagga 2880
cattctccgg gttggggtca ctttggctgg ccaccagaaa aaaatcctga acagtatcca 2940
ggtgatgcgg gcgcagatga accagattca gtctgtggag ggccagccac tcgccaggag 3000
gccacgggcc acgggaagaa ccaagcggtg ccagccacga gacgtcacca agaaaacatg 3060
caactcaaac gacggaaaaa aaaagggaat gggaaaaaag aaaacagatc ctgggagggg 3120
gcgggaaata caaggaatat tttttaaaga ggattctcat aaggaaagca atgactgttc 3180
ttgcgggggа taaaaaaggg cttgggagat tcatgcgatg tgtccaatcg gagacaaaag 3240
cagtttctct ccaactccct ctgggaaggt gacctggcca gagccaagaa acactttcag 3300
aaaaacaaat gtgaagggga gagacagggg ccacccttgg ctcctgtccc tgctgctcct 3360
ctaggcctca ctcaacaacc aagcgcctgg aggacgggac agatggacag acagccaccc 3420
tgagaacccc tctgggaaaa tctattcctg ccaccactgg gcaaacagaa gaatttttct 3480
gtctttggag agtattttag aaactccaat gaaagacact gtttctcctg ttggctcaca 3540
gggctgaaag gggcttttgt cctcctgggt cagggagaac gcggggaccc cagaaaggtc 3600
agccttcctg aggatgggca acccccaggt ctgcagctcc aggtacatat cacgcgcaca 3660
gcctggcagc ctggccctcc tggtgcccac tcccgccagc ccctgcctcg aggactgata 3720
ctgcagtgac tgccgtcagc tccgactgcc gctgagaagg gttgatcctg catctgggtt 3780
tgtttacagc aattcctgga ctcgggggta ttttggtcac agggtggttt tggtttaggg 3840
ggtttgtttg ttgggttgtt ttttgttttt tggttttttt taatgacaat gaagtgacac 3900
tttgacattt ccaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 3949

<210> 237
<211> 4234
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004443
<309> 2004-11-16

<400> 237
cgtgagcggc gcagcaagat cccagctcgg accccggacg gcgcgcgccc ccgaagcccc 60
ggatcccagt cgggcccgca gctgaccgcc agattactgt gcatcccgaa tcacgaccac 120
ctgcaccctc ctgccccggc ccgcccccca agtcctcagg cacccagctc cccggcgccc 180
cggatcctcc tggaccggtc cgtccagatt cccgcgggac cgacctgtcc gcatccccag 240
gaccgccggg ctcggtgcac cgcctcggtc ccggagccgc ccgcctggat tgcattccct 300
cctctcctgg atctcctggg acccgacgcg agcctgcccc ggagcccgcc gagcgcaccc 360
tctctcgggt gcctgcagcc ccgccggcgc ggcccggccc ggcgcggccc ggctcggctc 420
ctagagctgc cacggccatg gccagagccc gcccgccgcc gccgccgtcg ccgccgccgg 480
ggcttctgcc gctgctccct ccgctgctgc tgctgccgct gctgctgctg cccgccggct 540
gccgggcgct ggaagagacc ctcatggaca caaaatgggt aacatctgag ttggcgtgga 600
catctcatcc agaaagtggg tgggaagagg tgagtggcta cgatgaggcc atgaatccca 660
tccgcacata ccaggtgtgt aatgtgcgcg agtcaagcca gaacaactgg cttcgcacgg 720
ggttcatctg gcggcgggat gtgcagcggg tctacgtgga gctcaagttc actgtgcgtg 780
actgcaacag catccccaac atccccggct cctgcaagga gaccttcaac ctcttctact 840
acgaggctga cagcgatgtg gcctcagcct cctccccctt ctggatggag aacccctacg 900
tgaaagtgga caccattgca cccgatgaga gcttctcgcg gctggatgcc ggccgtgtca 960
acaccaaggt gcgcagcttt gggccacttt ccaaggctgg cttctacctg gccttccagg 1020

accagggcgc ctgcatgtcg ctcatctccg tgcgcgcctt ctacaagaag tgtgcatcca 1080
ccaccgcagg cttcgcactc ttccccgaga ccctcactgg ggcggagccc acctcgctgg 1140
tcattgctcc tggcacctgc atccctaacg ccgtggaggt gtcggtgcca ctcaagctct 1200
actgcaacgg cgatggggag tggatggtgc ctgtgggtgc ctgcacctgt gccaccggcc 1260
atgagccagc tgccaaggag tcccagtgcc gcccctgtcc ccctgggagc tacaaggcga 1320
agcagggaga ggggcccctgc ctcccatgtc cccccaacag ccgtaccacc tccccagccg 1380
ccagcatctg cacctgccac aataacttct accgtgcaga ctcggactct gcggacagtg 1440
cctgtaccac cgtgccatct ccaccccgag gtgtgatctc caatgtgaat gaaacctcac 1500
tgatcctcga gtggagtgag ccccgggacc tgggtggccg ggatgacctc ctgtacaatg 1560
tcatctgcaa gaagtgccat ggggctggag gggcctcagc ctgctcacgc tgtgatgaca 1620
acgtggagtt tgtgcctcgg cagctgggcc tgacggagcg ccgggtccac atcagccatc 1680
tgctggccca cacgcgctac acctttgagg tgcaggcggt caacggtgtc tcgggcaaga 1740
gccctctgcc gcctcgttat gcggccgtga atatcaccac aaaccaggct gccccgtctg 1800
aagtgcccac actacgcctg cacagcagct caggcagcag cctcacccta tcctgggcac 1860
ccccagagcg gcccaacgga gtcatcctgg actacgagat gaagtacttt gagaagagcg 1920
agggcatcgc ctccacagtg accagccaga tgaactccgt gcagctggac gggcttcggc 1980
ctgacgcccg ctatgtggtc caggtccgtg cccgcacagt agctggctat gggcagtaca 2040
gccgccctgc cgagtttgag accacaagtg agagaggctc tggggcccag cagctccagg 2100
agcagcttcc cctcatcgtg ggctccgcta cagctgggct tgtcttcgtg gtggctgtcg 2160
tggtcatcgc tatcgtctgc ctcaggaagc agcgacacgg ctctgattcg gagtacacgg 2220
agaagctgca gcagtacatt gctcctggaa tgaaggttta tattgaccct tttacctacg 2280
aggaccctaa tgaggctgtt cgggagtttg ccaaggagat cgacgtgtcc tgcgtcaaga 2340
tcgaggaggt gatcggagct ggggaatttg gggaagtgtg ccgtggtcga ctgaaacagc 2400
ctggccgccg agaggtgttt gtggccatca agacgctgaa ggtgggctac accgagaggc 2460
agcggcggga cttcctaagc gaggcctcca tcatgggtca gtttgatcac cccaatataa 2520
tccggctcga gggcgtggtc accaaaagtc ggccagttat gatcctcact gagttcatgg 2580
aaaactgcgc cctggactcc ttcctccggc tcaacgatgg gcagttcacg gtcatccagc 2640
tggtgggcat gttgcggggc attgctgccg gcatgaagta cctgtccgag atgaactatg 2700
tgcaccgcga cctggctgct cgcaacatcc ttgtcaacag caacctggtc tgcaaagtct 2760
cagactttgg cctctcccgc ttcctggagg atgacccctc cgatcctacc tacaccagtt 2820
ccctgggcgg gaagatcccc atccgctgga ctgccccaga ggccatagcc tatcggaagt 2880
tcacttctgc tagtgatgtc tggagctacg gaattgtcat gtgggaggtc atgagctatg 2940
gagagcgacc ctactgggac atgagcaacc aggatgtcat caatgccgtg gagcaggatt 3000
accggctgcc accacccatg gactgtccca cagcactgca ccagctcatg ctggactgct 3060
gggtgcggga ccggaacctc aggcccaaat tctcccagat tgtcaatacc ctggacaagc 3120
tcatccgcaa tgctgccagc ctcaaggtca ttgccagcgc tcagtctggc atgtcacagc 3180
ccctcctgga ccgcacggtc ccagattaca caaccttcac gacagttggt gattggctgg 3240
atgccatcaa gatggggcgg tacaaggaga gcttcgtcag tgcggggttt gcatcttttg 3300
acctggtggc ccagatgacg gcagaagacc tgctccgtat tggggtcacc ctggccggcc 3360
accagaagaa gatcctgagc agtatccagg acatgcggct gcagatgaac cagacgctgc 3420
ctgtgcaggt ctgacaccgg ctcccacggg gaccctgagg accgtgcagg gatgccaagc 3480
agccggctgg actttcggac tcttggactt ttggatgcct ggccttaggc tgtggcccag 3540
aagctggaag tttgggaaag gcccaagctg ggacttctcc aggcctgtgt tccctcccca 3600
ggaagtgcgc cccaaacctc ttcatattga agatggatta ggagaggggg tgatgacccc 3660
tccccaagcc cctcagggcc cagaccttcc tgctctccag caggggatcc ccacaacctc 3720
acacttgtct gttcttcagt gctggaggtc ctggcagggt caggctgggg taagccgggg 3780
ttccacaggg cccagccctg gcaggggtct ggcccccccag gtaggcggag agcagtccct 3840
ccctcaggaa ctggaggagg ggactccagg aatggggaaa tgtgacacca ccatcctgaa 3900
gccagcttgc acctccagtt tgcacaggga tttgttctgg gggctgaggg ccctgtcccc 3960
acccccgccc ttggtgctgt cataaaaggg caggcagggg caggctgagg agttgccctt 4020
tgccccccag agactgactc tcagagccag agatgggatg tgtgagtgtg tgtgtgtgtg 4080
tgtgtgtgtg cgcgcgcgcg cgcgtgtgtg tgtgcacgca ctggcctgca cagagagcat 4140
gggtgagcgt gtaaaagctt ggccctgtgc cctacaatgg ggccagctgg gccgacagca 4200
gaataaaggc aataagatga aaaaaaaaaa aaaa 4234

<210> 238

<211> 4369
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004444
<309> 2004-11-16

<400> 238
ttccagcgca gctcagcccc tgcccggccc ggcccgcccg gctccgcgcc gcagtctccc 60
tccctcccgc tccgtccccg ctcgggctcc caccatcccc gcccgcgagg agagcactcg 120
gcccggcggc gcgagcagag ccactccagg gagggggga gaccgcgagc ggccggctca 180
gcccccgcca cccggggcgg gaccccgagg ccccggaggg accccaactc cagccacgtc 240
ttgctgcgcg cccgcccggc gcggccactg ccagcacgct ccgggcccgc cgcccgcgcg 300
cgcggcacag acgcggggcc acacttggcg ccgccgcccg gtgccccgca cgctcgcatg 360
ggcccgcgct gagggccccg acgaggagtc ccgcgcggag tatcggcgtc cacccgccca 420
gggagagtca gacctggggg ggcgagggcc ccccaaactc agttcggatc ctacccgagt 480
gaggcggcgc catggagctc cgggtgctgc tctgctgggc ttcgttggcc gcagctttgg 540
aagagaccct gctgaacaca aaattggaaa ctgctgatct gaagtgggtg acattccctc 600
aggtggacgg gcagtgggag gaactgagcg gcctggatga ggaacagcac agcgtgcgca 660
cctacgaagt gtgtgacgtg cagcgtgccc cgggccaggc ccactggctt cgcacaggtt 720
gggtcccacg gcggggcgcc gtccacgtgt acgccacgct gcgcttcacc atgctcgagt 780
gcctgtccct gcctcgggct gggcgctcct gcaaggagac cttcaccgtc ttctactatg 840
agagcgatgc ggacacggcc acggccctca cgccagcctg gatggagaac ccctacatca 900
aggtggacac ggtggccgcg gagcatctca cccggaagcg ccctggggcc gaggccaccg 960
ggaaggtgaa tgtcaagacg ctgcgtctgg gaccgctcag caaggctggc ttctacctgg 1020
ccttccagga ccagggtgcc tgcatggccc tgctatccct gcacctcttc tacaaaaagt 1080
gcgcccagct gactgtgaac ctgactcgat tcccggagac tgtgcctcgg gagctggttg 1140
tgcccgtggc cggtagctgc gtggtggatg ccgtccccgc ccctggcccc agccccagcc 1200
tctactgccg tgaggatggc cagtgggccg aacagccggt cacgggctgc agctgtgctc 1260
cggggttcga ggcagctgag gggaacacca agtgccgagc ctgtgcccag ggcaccttca 1320
agcccctgtc aggagaaggg tcctgccagc catgcccagc caatagccac tctaacacca 1380
ttggatcagc cgtctgccag tgccgcgtcg ggtacttccg ggcacgcaca gacccccggg 1440
gtgcaccctg caccaccctt ccttcggctc cgcggagcgt ggtttcccgc ctgaacggct 1500
cctccctgca cctggaatgg agtgcccccc tggagtctgg tggccgagag gacctcacct 1560
acgccctccg ctgccgggag tgccgacccg gaggctcctg tgcgccctgc gggggagacc 1620
tgacttttga ccccggcccc cgggacctgg tggagccctg ggtggtggtt cgagggctac 1680
gtcctgactt cacctatacc tttgaggtca ctgcattgaa cggggtatcc tccttagcca 1740
cggggcccgt cccatttgag cctgtcaatg tcaccactga ccgagaggta cctcctgcag 1800
tgtctgacat ccgggtgacg cggtcctcac ccagcagctt gagcctggcc tgggctgttc 1860
cccgggcacc cagtggggct gtgctggact acgaggtcaa ataccatgag aagggcgccg 1920
agggtcccag cagcgtgcgg ttcctgaaga cgtcagaaaa ccgggcagag ctgcgggggc 1980
tgaagcgggg agccagctac ctggtgcagg tacgggcgcg ctctgaggcc ggctacgggc 2040
ccttcggcca ggaacatcac agccagaccc aactggatga gagcgagggc tggcgggagc 2100
agctggccct gattgcgggc acggcagtcg tgggtgtggt cctggtcctg gtggtcattg 2160
tggtcgcagt tctctgcctc aggaagcaga gcaatgggag agaagcagaa tattcggaca 2220
aacacggaca gtatctcatc ggacatggta ctaaggtcta catcgacccc ttcacttatg 2280
aagaccctaa tgaggctgtg agggaatttg caaaagagat cgatgtctcc tacgtcaaga 2340
ttgaagaggt gattggtgca ggtgagtttg gcgaggtgtg ccgggggcgg ctcaaggccc 2400
cagggaagaa ggagagctgt gtggcaatca agaccctgaa gggtggctac acggagcggc 2460
agcggcgtga gtttctgagc gaggcctcca tcatgggcca gttcgagcac cccaatatca 2520
tccgcctgga gggcgtggtc accaacagca tgcccgtcat gattctcaca gagttcatgg 2580
agaacggcgc cctggactcc ttcctgcggc taaacgacgg acagttcaca gtcatccagc 2640
tcgtgggcat gctgcggggc atcgcctcgg gcatgcggta ccttgccgag atgagctacg 2700
tccaccgaga cctggctgct cgcaacatcc tagtcaacag caacctcgtc tgcaaagtgt 2760
ctgactttgg cctttcccga ttcctggagg agaactcttc cgatcccacc tacacgagct 2820

ccctgggagg aaagattccc atccgatgga ctgccccgga ggccattgcc ttccggaagt 2880
tcacttccgc cagtgatgcc tggagttacg ggattgtgat gtgggaggtg atgtcatttg 2940
gggagaggcc gtactgggac atgagcaatc aggacgtgat caatgccatt gaacaggact 3000
accggctgcc cccgccccca gactgtccca cctccctcca ccagctcatg ctggactgtt 3060
ggcagaaaga ccggaatgcc cggccccgct tcccccaggt ggtcagcgcc ctggacaaga 3120
tgatccggaa ccccgccagc ctcaaaatcg tggcccggga gaatggcggg gcctcacacc 3180
ctctcctgga ccagcggcag cctcactact cagcttttgg ctctgtgggc gagtggcttc 3240
gggccatcaa aatgggaaga tacgaagaaa gtttcgcagc cgctggcttt ggctccttcg 3300
agctggtcag ccagatctct gctgaggacc tgctccgaat cggagtcact ctggcgggac 3360
accagaagaa aatcttggcc agtgtccagc acatgaagtc ccaggccaag ccgggaaccc 3420
cgggtgggac aggaggaccg gccccgcagt actgacctgc aggaactccc caccccaggg 3480
acaccgcctc cccatttttcc ggggcagagt ggggactcac agaggccccc agccctgtgc 3540
cccgctggat tgcactttga gcccgtgggg tgaggagttg gcaatttgga gagacaggat 3600
ttgggggttc tgccataata ggaggggaaa atcacccccc agccacctcg gggaactcca 3660
gaccaagggt gagggcgcct ttccctcagg actgggtgtg accagaggaa aaggaagtgc 3720
ccaacatctc ccagcctccc caggtgcccc cctcaccttg atgggtgcgt tcccgcagac 3780
caaagagagt gtgactccct tgccagctcc agagtggggg ggctgtccca gggggcaaga 3840
aggggtgtca gggcccagtg acaaaatcat tggggtttgt agtcccaact tgctgctgtc 3900
accaccaaac tcaatcattt ttttcccttg taaatgcccc tcccccagct gctgccttca 3960
tattgaaggt ttttgagttt tgtttttggt cttaattttt ctccccgttc ccttttgtt 4020
tcttcgtttt gtttttctac cgtccttgtc ataactttgt gttggaggga acctgtttca 4080
ctatggcctc ctttgcccaa gttgaaacag gggcccatca tcatgtctgt ttccagaaca 4140
gtgccttggt catcccacat ccccggaccc cgcctgggac ccccaagctg tgtcctatga 4200
aggggtgtgg ggtgaggtag tgaaaagggc ggtagttggt ggtggaaccc agaaacggac 4260
gccggtgctt ggaggggttc ttaaattata tttaaaaaag taacttttg tataaataaa 4320
agaaaatggg acgtgtccca gctccagggg taaaaaaaaa aaaaaaaaa 4369

<210> 239
<211> 4059
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004445
<309> 2004-11-29

<400> 239
ggggcgggcc gggccggctt gggaggggac gcggaggggg cgggccgggc tgcgttcgct 60
ccagccgcgg ctctacagca gcgggcggcg ggacccggga cccagcttgg cgacggcgat 120
ctcgacgcgg gccccccagga tctcccggcg ccccacctct ggagcagccc ctgccgccag 180
cgtcaggtcc accccggaat cccagggact ctcggcgccg aacggacccg ggccgggtgc 240
aacggggtcc ccggactgga gaagacgcgg gtggcaccgt gcgagctcca ggagccccgg 300
gtccactgcg aggcctcggg gggcgcagac ctgcagagac tgcggccaac gggaagaaat 360
aaagggatta tagtccaccc aattcacaga cttctgagac tcagacacga ggagagatag 420
agaaccgcca atctctagat caacaagcaa aggaggtgcc aagcctgttt gtcttcattg 480
tgacactgga gtctagatgc tgggaagtcc aagatcaggg tgccggcatg gtcagttcct 540
ggcgaagcct ctcttctagg tttcagactg ccctcttctt tgttgtgtcc tcgaatggca 600
gaaaaagggg tggctgttgg aggaagggag gagagtaaat gaagagaaag aactggaata 660
acccccttgca gaaaaaaaaa aaaagggaag caagcttagc tgtacaccct gagtcttgca 720
aaagctgcag ccccacccag gagcagggtg gtggctgggg cgatggtgga cgccctgaag 780
atgtcccatg gctactgaag gggctgccca gttagggaac agagtggcgg gcatggtgtg 840
tagcctatgg gtgctgctcc tggtgtcttc agttctggct ctggaagagg tattgctgga 900
caccaccgga gagacatctg agattggctg gctcacctac ccaccagggg ggtgggacga 960
ggtgagtgtt ctggacgacc agcgacgcct gactcggacc tttgaggcat gtcatgtggc 1020
aggggcccct ccaggcaccg ggcaggacaa ttggttgcag acacactttg tggagcggcg 1080
cggggcccag agggcgcaca ttcgactcca cttctctgtg cgggcatgct ccagcctggg 1140

tgtgagcggc ggcacctgcc gggagacctt cacccttтac taccgtcagg ctgaggagcc 1200
cgacagccct gacagcgttt cctcctggca cctcaaacgc tggaccaagg tggacacaat 1260
tgcagcagac gagagctttc cctcctcctc ctcctcctcc tcctcttctt cctctgcagc 1320
gtgggctgtg ggaccccacg gggctgggca gcgggctgga ctgcaactga acgtcaaaga 1380
gcggagcttt gggcctctca cccaacgcgg cttctacgtg gccttccagg acacgggggc 1440
ctgcctggcc ctggtcgctg tcaggctctt ctcctacacc tgccctgccg tgctccgatc 1500
ctttgcttcc tttccagaga cgcaggccag tggggctggg ggggcctccc tggtggcagc 1560
tgtgggcacc tgtgtggctc atgcagagcc agaggaggat ggagtagggg gccaggcagg 1620
aggcagcccc cccaggctgc actgcaacgg ggagggcaag tggatggtag ctgtcggggg 1680
ctgccgctgc cagcctggat accaaccagc acgaggagac aaggcctgcc aagcctgccc 1740
acgggggctc tataagtctt ctgctgggaa tgctccctgc tcaccatgcc ctgcccgcag 1800
tcacgctccc aacccagcag cccccgtttg cccctgcctg gagggcttct accgggccag 1860
ttccgaccca ccagaggccc cctgcactgg tcctccatcg gctccccagg agctttggtt 1920
tgaggtgcaa ggctcagcac tcatgctaca ctggcgcctg cctcgggagc tgggggtcg 1980
aggggacctg ctcttcaatg tcgtgtgcaa ggagtgtgaa ggccgccagg aacctgccag 2040
cggtggtggg ggcacttgtc accgctgcag ggatgaggtc cacttcgacc ctcgccagag 2100
aggcctgact gagagccgag tgttagtggg gggactccgg gcacacgtac cctacatctt 2160
agaggtgcag gctgttaatg gggtgtctga gctcagccct gaccctcctc aggctgcagc 2220
catcaatgtc agcaccagcc atgaagtgcc ctctgctgtc cctgtggtgc accaggtgag 2280
ccgggcatcc aacagcatca cggtgtcctg gccgcagccc gaccagacca atgggaacat 2340
cctggactat cagctccgct actatgacca ggcagaagac gaatcccact ccttcaccct 2400
gaccagcgag accaacactg ccaccgtgac acagctgagc cctggccaca tctatggttt 2460
ccaggtgcgg gcccggactg ctgccggcca cggcccctac gggggcaaag tctatttcca 2520
gacacttcct caaggggagc tgtcttccca gcttccggaa agactctcct tggtgatcgg 2580
ctccatcctg ggggctttgg ccttcctcct gctggcagcc atcaccgtgc tggcggtcgt 2640
cttccagcgg aagcggcgtg ggactggcta cacggagcag ctgcagcaat acagcagccc 2700
aggactcggg gtgaagtatt acatcgaccc ctccacctac gaggacccct gtcaggccat 2760
ccgagaactt gcccgggaag tcgatcctgc ttatatcaag attgaggagg tcattgggac 2820
aggctctttt ggagaagtgc gccagggccg cctgcagcca cggggacgga gggagcagac 2880
tgtggccatc caggccctgt gggccggggg cgccgaaagc ctgcagatga ccttcctggg 2940
ccgggccgca gtgctgggtc agttccagca ccccaacatc ctgcggctgg agggcgtggt 3000
caccaagagc cgacccctca tggtgctgac ggagttcatg gagcttggcc ccctggacag 3060
cttcctcagg cagcgggagg gccagttcag cagcctgcag ctggtggcca tgcagcgggg 3120
agtggctgct gccatgcagt acctgtccag ctttgccttc gtccatcgct cgctgtctgc 3180
ccacagcgtg ctggtgaata gccacttggt gtgcaaggtg gcccgtcttg gccacagtcc 3240
tcagggccca agttgtttgc ttcgctgggc agccccagag gtcattgcac atggaaagca 3300
tacaacatcc agtgatgtct ggagctttgg gatactcatg tgggaagtga tgagttatgg 3360
agaacggcct tactgggaca tgagtgagca ggaggtacta aatgcaatag agcaggagtt 3420
ccggctgccc ccgcctccag gctgtcctcc tggattacat ctacttatgt tggacacttg 3480
gcagaaggac cgtgcccggc ggcctcattt tgaccagctg gtggctgcat ttgacaagat 3540
gatccgcaag ccagataccc tgcaggctgg cggggaccca ggggaaaggc cttcccaggc 3600
ccttctgacc cctgtggccc tggactttcc ttgtctggac tcaccccagg cctggctttc 3660
agccattgga ctggagtgct accaggacaa cttctccaag tttggcctct gtaccttcag 3720
tgatgtggct cagctcagcc tagaagacct gcctgccctg ggcatcaccc tggctggcca 3780
ccagaagaag ctgctgcacc acatccagct ccttcagcaa cacctgaggc agcagggctc 3840
agtggaggtc tgagaatgac gatacccgtg actcagccct ggacactggt ccgagaaggg 3900
acatgtggga cgtgagccgg gctccaacag cctctgtgag agatgcccca caccaaaccc 3960
aaccctcccg atggctgcat tccctggtcc tccgcctctc caccagcccc ctcctcatta 4020
aagggaaaga agggaatttg caaaaaaaaa aaaaaaaaa 4059

<210> 240
<211> 4624
<212> DNA
<213> Homo sapiens

<300>

<308> GenBank No. NM004448
<309> 2004-12-20

<400> 240
ggaggaggtg gaggaggagg gctgcttgag gaagtataag aatgaagttg tgaagctgag 60
attcccctcc attgggaccg gagaaaccag gggagccccc cgggcagccg cgcgcccctt 120
cccacggggc cctttactgc gccgcgcgcc cggcccccac ccctcgcagc accccgcgcc 180
ccgcgccctc ccagccgggt ccagccggag ccatggggcc ggagccgcag tgagcaccat 240
ggagctggcg gccttgtgcc gctgggggct cctcctcgcc ctcttgcccc ccggagccgc 300
gagcacccaa gtgtgcaccg gcacagacat gaagctgcgg ctccctgcca gtcccgagac 360
ccacctggac atgctccgcc acctctacca gggctgccag gtggtgcagg gaaacctgga 420
actcacctac ctgcccacca atgccagcct gtccttcctg caggatatcc aggaggtgca 480
gggctacgtg ctcatcgctc acaaccaagt gaggcaggtc ccactgcaga ggctgcggat 540
tgtgcgaggc acccagctct ttgaggacaa ctatgccctg gccgtgctag acaatggaga 600
cccgctgaac aataccaccc ctgtcacagg ggcctcccca ggaggcctgc gggagctgca 660
gcttcgaagc ctcacagaga tcttgaaagg aggggtcttg atccagcgga acccccagct 720
ctgctaccag gacacgattt tgtggaagga catcttccac aagaacaacc agctggctct 780
cacactgata gacaccaacc gctctcgggc ctgccacccc tgttctccga tgtgtaaggg 840
ctcccgctgc tggggagaga gttctgagga ttgtcagagc ctgacgcgca ctgtctgtgc 900
cggtggctgt gcccgctgca aggggccact gcccactgac tgctgccatg agcagtgtgc 960
tgccggctgc acgggcccca agcactctga ctgcctggcc tgcctccact tcaaccacag 1020
tggcatctgt gagctgcact gcccagccct ggtcacctac aacacagaca cgtttgagtc 1080
catgcccaat cccgagggcc ggtatacatt cggcgccagc tgtgtgactg cctgtcccta 1140
caactacctt tctacggacg tgggatcctg caccctcgtc tgccccctgc acaaccaaga 1200
ggtgacagca gaggatggaa cacagcggtg tgagaagtgc agcaagccct gtgcccgagt 1260
gtgctatggt ctgggcatgg agcacttgcg agaggtgagg gcagttacca gtgccaatat 1320
ccaggagttt gctggctgca agaagatctt tgggagcctg gcatttctgc cggagagctt 1380
tgatggggac ccagcctcca acactgcccc gctccagcca gagcagctcc aagtgtttga 1440
gactctggaa gagatcacag gttacctata catctcagca tggccggaca gcctgcctga 1500
cctcagcgtc ttccagaacc tgcaagtaat ccggggacga attctgcaca atggcgccta 1560
ctcgctgacc ctgcaagggc tgggcatcag ctggctgggg ctgcgctcac tgagggaact 1620
gggcagtgga ctggccctca tccaccataa cacccacctc tgcttcgtgc acacggtgcc 1680
ctgggaccag ctctttcgga acccgcacca agctctgctc cacactgcca accggccaga 1740
ggacgagtgt gtgggcgagg gcctggcctg ccaccagctg tgcgcccgag ggcactgctg 1800
gggtccaggg cccacccagt gtgtcaactg cagccagttc cttcggggcc aggagtgcgt 1860
ggaggaatgc cgagtactgc aggggctccc cagggagtat gtgaatgcca ggcactgttt 1920
gccgtgccac cctgagtgtc agccccagaa tggctcagtg acctgttttg gaccggaggc 1980
tgaccagtgt gtggcctgtg cccactataa ggaccctccc ttctgcgtgg cccgctgccc 2040
cagcggtgtg aaacctgacc tctcctacat gcccatctgg aagtttccag atgaggaggg 2100
cgcatgccag ccttgcccca tcaactgcac ccactcctgt gtggacctgg atgacaaggg 2160
ctgccccgcc gagcagagag ccagccctct gacgtccatc atctctgcgg tggttggcat 2220
tctgctggtc gtggtcttgg gggtggtctt tgggatcctc atcaagcgac ggcagcagaa 2280
gatccggaag tacacgatgc ggagactgct gcaggaaacg gagctggtgg agccgctgac 2340
acctagcgga gcgatgccca accaggcgca gatgcggatc ctgaaagaga cggagctgag 2400
gaaggtgaag gtgcttggat ctggcgcttt tggcacagtc tacaagggca tctggatccc 2460
tgatggggag aatgtgaaaa ttccagtggc catcaaagtg ttgagggaaa acacatcccc 2520
caaagccaac aaagaaatct tagacgaagc atacgtgatg gctggtgtgg gctccccata 2580
tgtctcccgc cttctgggca tctgcctgac atccacggtg cagctggtga cacagcttat 2640
gccctatggc tgcctcttag accatgtccg ggaaaaccgc ggacgcctgg gctcccagga 2700
cctgctgaac tggtgtatgc agattgccaa ggggatgagc tacctggagg atgtgcggct 2760
cgtacacagg gacttggccg ctcggaacgt gctggtcaag agtcccaacc atgtcaaaat 2820
tacagacttc gggctggctc ggctgctgga cattgacgag acagagtacc atgcagatgg 2880
gggcaaggtg cccatcaagt ggatggcgct ggagtccatt ctccgccggc ggttcaccca 2940
ccagagtgat gtgtggagtt atggtgtgac tgtgtgggag ctgatgactt ttggggccaa 3000
accttacgat gggatcccag cccgggagat ccctgacctg ctggaaaagg gggagcggct 3060
gccccagccc cccatctgca ccattgatgt ctacatgatc atggtcaaat gttggatgat 3120

tgactctgaa tgtcggccaa gattccggga gttggtgtct gaattctccc gcatggccag 3180
ggacccccag cgctttgtgg tcatccagaa tgaggacttg ggcccagcca gtcccttgga 3240
cagcaccttc taccgctcac tgctggagga cgatgacatg ggggacctgg tggatgctga 3300
ggagtatctg gtaccccagc agggcttctt ctgtccagac cctgccccgg gcgctggggg 3360
catggtccac cacaggcacc gcagctcatc taccaggagt ggcggtgggg acctgacact 3420
agggctggag ccctctgaag aggaggcccc caggtctcca ctggcaccct ccgaaggggc 3480
tggctccgat gtatttgatg gtgacctggg aatgggggca gccaaggggc tgcaaagcct 3540
ccccacacat gaccccagcc ctctacagcg gtacagtgag gaccccacag taccctgcc 3600
ctctgagact gatggctacg ttgccccccc gacctgcagc ccccagcctg aatatgtgaa 3660
ccagccagat gttcggcccc agccccccttc gccccgagag ggccctctgc ctgctgcccg 3720
acctgctggt gccactctgg aaaggcccaa gactctctcc ccagggaaga atggggtcgt 3780
caaagacgtt tttgcctttg ggggtgccgt ggagaacccc gagtacttga caccccaggg 3840
aggagctgcc cctcagcccc accctcctcc tgccttcagc ccagccttcg acaacctcta 3900
ttactgggac caggacccac cagagcgggg ggctccaccc agcaccttca aagggacacc 3960
tacggcagag aacccagagt acctgggtct ggacgtgcca gtgtgaacca gaaggccaag 4020
tccgcagaag ccctgatgtg tcctcaggga gcagggaagg cctgacttct gctggcatca 4080
agaggtggga gggccctccg accacttcca ggggaacctg ccatgccagg aacctgtcct 4140
aaggaacctt ccttcctgct tgagttccca gatggctgga aggggtccag cctcgttgga 4200
agaggaacag cactggggag tctttgtgga ttctgaggcc ctgcccaatg agactctagg 4260
gtccagtgga tgccacagcc cagcttggcc ctttccttcc agatcctggg tactgaaagc 4320
cttagggaag ctggcctgag aggggaagcg gccctaaggg agtgtctaag aacaaaagcg 4380
acccattcag agactgtccc tgaaacctag tactgccccc catgaggaag gaacagcaat 4440
ggtgtcagta tccaggcttt gtacagagtg cttttctgtt tagtttttac ttttttttgtt 4500
ttgttttttt aaagatgaaa taaagaccca gggggagaat gggtgttgta tggggaggca 4560
agtgtggggg gtccttctcc acacccactt tgtccatttg caaatatatt ttggaaaaca 4620
gcta 4624

<210> 241
<211> 5511
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM001982
<309> 2004-12-20

<400> 241
acacacacac acccctcccc tgccatccct ccccggactc cggctccggc tccgattgca 60
atttgcaacc tccgctgccg tcgccgcagc agccaccaat tcgccagcgg ttcaggtggc 120
tcttgcctcg atgtcctagc ctaggggccc ccgggccgga cttggctggg ctcccttcac 180
cctctgcgga gtcatgaggg cgaacgacgc tctgcaggtg ctgggcttgc ttttcagcct 240
ggcccggggc tccgaggtgg gcaactctca ggcagtgtgt cctgggactc tgaatggcct 300
gagtgtgacc ggcgatgctg agaaccaata ccagacactg tacaagctct acgagaggtg 360
tgaggtggtg atggggaacc ttgagattgt gctcacggga cacaatgccg acctctcctt 420
cctgcagtgg attcgagaag tgacaggcta tgtcctcgtg gccatgaatg aattctctac 480
tctaccattg cccaacctcc gcgtggtgcg agggacccag gtctacgatg ggaagtttgc 540
catcttcgtc atgttgaact ataacaccaa ctccagccac gctctgcgcc agctccgctt 600
gactcagctc accgagattc tgtcaggggg tgtttatatt gagaagaacg ataagctttg 660
tcacatggac acaattgact ggagggacat cgtgagggac cgagatgctg agatagtggt 720
gaaggacaat ggcagaagct gtccccccctg tcatgaggtt tgcaaggggc gatgctgggg 780
tcctggatca gaagactgcc agacattgac caagaccatc tgtgctcctc agtgtaatgg 840
tcactgcttt gggcccaacc ccaaccagtg ctgccatgat gagtgtgccg ggggctgctc 900
aggccctcag gacacagact gctttgcctg ccggcacttc aatgacagtg gagcctgtgt 960
acctcgctgt ccacagcctc ttgtctacaa caagctaact ttccagctgg aacccaatcc 1020
ccacaccaag tatcagtatg gaggagtttg tgtagccagc tgtccccata actttgtggt 1080
ggatcaaaca tcctgtgtca gggcctgtcc tcctgacaag atggaagtag ataaaaatgg 1140

gctcaagatg tgtgagcctt gtgggggact atgtcccaaa gcctgtgagg gaacaggctc 1200
tgggagccgc ttccagactg tggactcgag caacattgat ggatttgtga actgcaccaa 1260
gatcctgggc aacctggact ttctgatcac cggcctcaat ggagacccct ggcacaagat 1320
ccctgccctg gacccagaga agctcaatgt cttccggaca gtacgggaga tcacaggtta 1380
cctgaacatc cagtcctggc cgccccacat gcacaacttc agtgtttttt ccaatttgac 1440
aaccattgga ggcagaagcc tctacaaccg gggcttctca ttgttgatca tgaagaactt 1500
gaatgtcaca tctctgggct tccgatccct gaaggaaatt agtgctgggc gtatctatat 1560
aagtgccaat aggcagctct gctaccacca ctctttgaac tggaccaagg tgcttcgggg 1620
gcctacggaa gagcgactag acatcaagca taatcggccg cgcagagact gcgtggcaga 1680
gggcaaagtg tgtgacccac tgtgctcctc tgggggatgc tggggcccag gccctggtca 1740
gtgcttgtcc tgtcgaaatt atagccgagg aggtgtctgt gtgacccact gcaactttct 1800
gaatggggag cctcgagaat ttgcccatga ggccgaatgc ttctcctgcc acccggaatg 1860
ccaacccatg gagggcactg ccacatgcaa tggctcgggc tctgatactt gtgctcaatg 1920
tgcccatttt cgagatgggc cccactgtgt gagcagctgc ccccatggag tcctaggtgc 1980
caagggccca atctacaagt acccagatgt tcagaatgaa tgtcggccct gccatgagaa 2040
ctgcacccag gggtgtaaag gaccagagct tcaagactgt ttaggacaaa cactggtgct 2100
gatcggcaaa acccatctga caatggcttt gacagtgata gcaggattgg tagtgatttt 2160
catgatgctg ggcggcactt ttctctactg gcgtgggcgc cggattcaga ataaaagggc 2220
tatgaggcga tacttggaac ggggtgagag catagagcct ctggacccca gtgagaaggc 2280
taacaaagtc ttggccagaa tcttcaaaga gacagagcta aggaagctta aagtgcttgg 2340
ctcgggtgtc tttggaactg tgcacaaagg agtgtggatc cctgagggtg aatcaatcaa 2400
gattccagtc tgcattaaag tcattgagga caagagtgga cggcagagtt ttcaagctgt 2460
gacagatcat atgctggcca ttggcagcct ggaccatgcc cacattgtaa ggctgctggg 2520
actatgccca gggtcatctc tgcagcttgt cactcaatat ttgcctctgg gttctctgct 2580
ggatcatgtg agacaacacc ggggggcact ggggccacag ctgctgctca actggggagt 2640
acaaattgcc aagggaatgt actaccttga ggaacatggt atggtgcata gaaacctggc 2700
tgcccgaaac gtgctactca agtcacccag tcaggttcag gtggcagatt ttggtgtggc 2760
tgacctgctg cctcctgatg ataagcagct gctatacagt gaggccaaga ctccaattaa 2820
gtggatggcc cttgagagta tccactttgg gaaatacaca caccagagtg atgtctggag 2880
ctatggtgtg acagtttggg agttgatgac cttcggggca gagccctatg cagggctacg 2940
attggctgaa gtaccagacc tgctagagaa gggggagcgg ttggcacagc cccagatctg 3000
cacaattgat gtctacatgg tgatggtcaa gtgttggatg attgatgaga acattcgccc 3060
aacctttaaa gaactagcca atgagttcac caggatggcc cgagacccac cacggtatct 3120
ggtcataaag agagagagtg ggcctggaat agcccctggg ccagagcccc atggtctgac 3180
aaacaagaag ctagaggaag tagagctgga gccagaacta gacctagacc tagacttgga 3240
agcagaggag gacaacctgg caaccaccac actgggctcc gccctcagcc taccagttgg 3300
aacacttaat cggccacgtg ggagccagag ccttttaagt ccatcatctg gatacatgcc 3360
catgaaccag ggtaatcttg gggagtcttg ccaggagtct gcagtttctg ggagcagtga 3420
acggtgcccc cgtccagtct ctctacaccc aatgccacgg ggatgcctgg catcagagtc 3480
atcagagggg catgtaacag gctctgaggc tgagctccag gagaaagtgt caatgtgtag 3540
gagccggagc aggagccgga gcccacggcc acgcggagat agcgcctacc attcccagcg 3600
ccacagtctg ctgactcctg ttaccccact ctccccaccc gggttagagg aagaggatgt 3660
caacggttat gtcatgccag atacacacct caaaggtact ccctcctccc gggaaggcac 3720
cctttcttca gtgggtctca gttctgtcct gggtactgaa gaagaagatg aagatgagga 3780
gtatgaatac atgaaccgga ggagaaggca cagtccacct catcccccta ggccaagttc 3840
ccttgaggag ctgggttatg agtacatgga tgtggggtca gacctcagtg cctctctggg 3900
cagcacacag agttgcccac tccaccctgt acccatcatg cccactgcag gcacaactcc 3960
agatgaagac tatgaatata tgaatcggca acgagatgga ggtggtcctg ggggtgatta 4020
tgcagccatg ggggcctgcc cagcatctga gcaagggtat gaagagatga gagcttttca 4080
ggggcctgga catcaggccc cccatgtcca ttatgcccgc ctaaaaactc tacgtagctt 4140
agaggctaca gactctgcct ttgataaccc tgattactgg catagcaggc ttttccccaa 4200
ggctaatgcc cagagaacgt aactcctgct ccctgtggca ctcagggagc atttaatggc 4260
agctagtgcc tttagagggt accgtcttct ccctattccc tctctctccc aggtcccagc 4320
ccctttcccc cagtcccaga caattccatt caatctttgg aggcttttaa acattttgac 4380
acaaaattct tatggtatgt agccagctgt gcactttctt ctctttccca accccaggaa 4440
aggttttcct tattttgtgt gctttcccag tcccattcct cagcttcttc acaggcactc 4500

ctggagatat gaaggattac tctccatatc ccttcctctc aggctcttga ctacttggaa 4560
ctaggctctt atgtgtgcct ttgtttccca tcagactgtc aagaagagga aagggaggaa 4620
acctagcaga ggaaagtgta attttggttt atgactctta acccccctaga aagacagaag 4680
cttaaaatct gtgaagaaag aggttaggag tagatattga ttactatcat aattcagcac 4740
ttaactatga gccaggcatc atactaaact tcacctacat tatctcactt agtcctttat 4800
catccttaaa acaattctgt gacatacata ttatctcatt ttacacaaag ggaagtcggg 4860
catggtggct catgcctgta atctcagcac tttgggaggc tgaggcagaa ggattacctg 4920
aggcaaggag tttgagacca gcttagccaa catagtaaga cccccatctc tttaaaaaaa 4980
aaaaaaaaaa aaaaaaaaaa actttagaac tgggtgcagt ggctcatgcc tgtaatccca 5040
gccagcactt tgggaggctg agatgggaag atcacttgag cccagaatta gagataagcc 5100
tatggaaaca tagcaagaca ctgtctctac aggggaaaaa aaaaaaagaa actgagcctt 5160
aaagagatga aataaattaa gcagtagatc caggatgcaa aatcctccca attcctgtgc 5220
atgtgctctt attgtaaggt gccaagaaaa actgatttaa gttacagccc ttgtttaagg 5280
ggcactgttt cttgtttttg cactgaatca agtctaaccc caacagccac atcctcctat 5340
acctagacat ctcatctcag gaagtggtgg tgggggtagt cagaaggaaa aataactgga 5400
catctttgtg taaaccataa tccacatgtg ccgtaaatga tcttcactcc ttatccgagg 5460
gcaaattcac aaggatcccc aagatccact tttagaagcc attctcatcc a 5511

<210> 242
<211> 4587
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM000141
<309> 2004-12-20

<400> 242
gagcgggcga gggagcgcgc gcggccgcca caaagctcgg gcgccgcggg gctgcatgcg 60
gcgtacctgg cccggcgcgg cgactgctct ccgggctggc gggggccggc cgcgagcccc 120
gggggccccg aggccgcagc ttgcctgcgc gctctgagcc ttcgcaactc gcgagcaaag 180
tttggtggag gcaacgccaa gcctgagtcc tttcttcctc tcgttcccca aatccgaggg 240
cagcccgcgg gcgtcatgcc cgcgctcctc cgcagcctgg ggtacgcgtg aagcccggga 300
ggcttggcgc cggcgaagac ccaaggacca ctcttctgcg tttggagttg ctccccacaa 360
ccccgggctc gtcgctttct ccatcccgac ccacgcgggg cgcggggaca acacaggtcg 420
cggaggagcg ttgccattca agtgactgca gcagcagcgg cagcgcctcg gttcctgagc 480
ccaccgcagg ctgaaggcat tgcgcgtagt ccatgcccgt agaggaagtg tgcagatggg 540
attaacgtcc acatggagat atggaagagg accggggatt ggtaccgtaa ccatggtcag 600
ctggggtcgt ttcatctgcc tggtcgtggt caccatggca accttgtccc tggcccggcc 660
ctccttcagt ttagttgagg ataccacatt agagccagaa gagccaccaa ccaaatacca 720
aatctctcaa ccagaagtgt acgtggctgc gccaggggag tcgctagagg tgcgctgcct 780
gttgaaagat gccgccgtga tcagttggac taaggatggg gtgcacttgg ggcccaacaa 840
taggacagtg cttattgggg agtacttgca gataaagggc gccacgccta gagactccgg 900
cctctatgct tgtactgcca gtaggactgt agacagtgaa acttggtact tcatggtgaa 960
tgtcacagat gccatctcat ccggagatga tgaggatgac accgatggtg cggaagattt 1020
tgtcagtgag aacagtaaca acaagagagc accatactgg accaacacag aaaagatgga 1080
aaagcggctc catgctgtgc ctgcggccaa cactgtcaag tttcgctgcc cagccggggg 1140
gaacccaatg ccaaccatgc ggtggctgaa aaacgggaag gagtttaagc aggagcatcg 1200
cattggaggc tacaaggtac gaaaccagca ctggagcctc attatggaaa gtgtggtccc 1260
atctgacaag ggaaattata cctgtgtggt ggagaatgaa tacgggtcca tcaatcacac 1320
gtaccacctg gatgttgtgg agcgatcgcc tcaccggccc atcctccaag ccggactgcc 1380
ggcaaatgcc tccacagtgg tcggaggaga cgtagagttt gtctgcaagg tttacagtga 1440
tgcccagccc cacatccagt ggatcaagca cgtggaaaag aacggcagta aatacgggcc 1500
cgacgggctg ccctacctca aggttctcaa ggccgccggt gttaacacca cggacaaaga 1560

gattgaggtt ctctatattc ggaatgtaac ttttgaggac gctggggaat atacgtgctt 1620
ggcgggtaat tctattggga tatcctttca ctctgcatgg ttgacagttc tgccagcgcc 1680
tggaagagaa aaggagatta cagcttcccc agactacctg gagatagcca tttactgcat 1740
aggggtcttc ttaatcgcct gtatggtggt aacagtcatc ctgtgccgaa tgaagaacac 1800
gaccaagaag ccagacttca gcagccagcc ggctgtgcac aagctgacca aacgtatccc 1860
cctgcggaga caggtaacag tttcggctga gtccagctcc tccatgaact ccaacacccc 1920
gctggtgagg ataacaacac gcctctcttc aacggcagac acccccatgc tggcaggggt 1980
ctccgagtat gaacttccag aggacccaaa atgggagttt ccaagagata agctgacact 2040
gggcaagccc ctgggagaag gttgctttgg gcaagtggtc atggcggaag cagtgggaat 2100
tgacaaagac aagcccaagg aggcggtcac cgtggccgtg aagatgttga aagatgatgc 2160
cacagagaaa gacctttctg atctggtgtc agagatggag atgatgaaga tgattgggaa 2220
acacaagaat atcataaatc ttcttggagc ctgcacacag gatgggcctc tctatgtcat 2280
agttgagtat gcctctaaag gcaacctccg agaatacctc cgagcccgga ggccacccgg 2340
gatggagtac tcctatgaca ttaaccgtgt tcctgaggag cagatgacct tcaaggactt 2400
ggtgtcatgc acctaccagc tggccagagg catggagtac ttggcttccc aaaaatgtat 2460
tcatcgagat ttagcagcca gaaatgtttt ggtaacagaa aacaatgtga tgaaaatagc 2520
agactttgga ctcgccagag atatcaacaa tatagactat tacaaaaaga ccaccaatgg 2580
gcggcttcca gtcaagtgga tggctccaga agccctgttt gatagagtat acactcatca 2640
gagtgatgtc tggtccttcg gggtgttaat gtgggagatc ttcactttag ggggctcgcc 2700
ctacccaggg attcccgtgg aggaactttt taagctgctg aaggaaggac acagaatgga 2760
taagccagcc aactgcacca acgaactgta catgatgatg agggactgtt ggcatgcagt 2820
gccctcccag agaccaacgt tcaagcagtt ggtagaagac ttggatcgaa ttctcactct 2880
cacaaccaat gaggaatact tggacctcag ccaacctctc gaacagtatt cacctagtta 2940
ccctgacaca agaagttctt gttcttcagg agatgattct gtttttctc cagaccccat 3000
gccttacgaa ccatgccttc ctcagtatcc acacataaac ggcagtgtta aaacatgaat 3060
gactgtgtct gcctgtcccc aaacaggaca gcactgggaa cctagctaca ctgagcaggg 3120
agaccatgcc tcccagagct tgttgtctcc acttgtatat atggatcaga ggagtaaata 3180
attggaaaag taatcagcat atgtgtaaag atttatacag ttgaaaactt gtaatcttcc 3240
ccaggaggag aagaaggttt ctggagcagt ggactgccac aagccaccat gtaacccctc 3300
tcacctgccg tgcgtactgg ctgtggacca gtaggactca aggtggacgt gcgttctgcc 3360
ttccttgtta attttgtaat aattggagaa gatttatgtc agcacacact tacagagcac 3420
aaatgcagta tataggtgct ggatgtatgt aaatatattc aaattatgta taaatatata 3480
ttatatattt acaaggagtt atttttgta ttgattttaa atggatgtcc caatgcacct 3540
agaaaattgg tctctctttt tttaatagct atttgctaaa tgctgttctt acacataatt 3600
tcttaatttt caccgagcag aggtggaaaa atacttttgc tttcagggaa aatggtataa 3660
cgttaattta ttaataaatt ggtaatatac aaaacaatta atcatttata gttttttttg 3720
taatttaagt ggcatttcta tgcaggcagc acagcagact agttaatcta ttgcttggac 3780
ttaactagtt atcagatcct ttgaaaagag aatatttaca atatatgact aatttgggga 3840
aaatgaagtt ttgatttatt tgtgtttaaa tgctgctgtc agacgattgt tcttagacct 3900
cctaaatgcc ccatattaaa agaactcatt cataggaagg tgtttcattt tggtgtgcaa 3960
ccctgtcatt acgtcaacgc aacgtctaac tggacttccc aagataaatg gtaccagcgt 4020
cctcttaaaa gatgccttaa tccattcctt gaggacagac cttagttgaa atgatagcag 4080
aatgtgcttc tctctggcag ctggccttct gcttctgagt tgcacattaa tcagattagc 4140
ctgattctct tcagtgaatt ttgataatgg cttccagact ctttgcgttg gagacgcctg 4200
ttaggatctt caagtcccat catagaaaat tgaaacacag agttgttctg ctgatagttt 4260
tggggatacg tccatctttt taagggattg ctttcatcta attctggcag gacctcacca 4320
aaagatccag cctcatacct acatcagaca aaatatcgcc gttgttcctt ctgtactaaa 4380
gtattgtgtt ttgctttgga aacacccact cactttgcaa tagccgtgca agatgaatgc 4440
agattacact gatcttatgt gttacaaaat tggagaaagt atttaataaa acctgttaat 4500
ttttatactg acaataaaaa tgtttctaca gatattaatg ttaacaagac aaaataaatg 4560
tcacgcaact taaaaaaaaa aaaaaaa 4587

<210> 243
<211> 4093
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM000142
<309> 2004-12-20

<400> 243
cgcgcgctgc ctgaggacgc cgcggccccc gcccccgcca tgggcgcccc tgcctgcgcc 60
ctcgcgctct gcgtggccgt ggccatcgtg gccggcgcct cctcggagtc cttggggacg 120
gagcagcgcg tcgtggggcg agcggcagaa gtcccgggcc cagagcccgg ccagcaggag 180
cagttggtct tcggcagcgg ggatgctgtg gagctgagct gtcccccgcc cgggggtggt 240
cccatggggc ccactgtctg ggtcaaggat ggcacagggc tggtgccctc ggagcgtgtc 300
ctggtggggc cccagcggct gcaggtgctg aatgcctccc acgaggactc cggggcctac 360
agctgccggc agcggctcac gcagcgcgta ctgtgccact tcagtgtgcg ggtgacagac 420
gctccatcct cgggagatga cgaagacggg gaggacgagg ctgaggacac aggtgtggac 480
acaggggccc cttactggac acggcccgag cggatggaca agaagctgct ggccgtgccg 540
gccgccaaca ccgtccgctt ccgctgccca gccgctggca accccactcc ctccatctcc 600
tggctgaaga acggcaggga gttccgcggc gagcaccgca ttggaggcat caagctgcgg 660
catcagcagt ggagcctggt catggaaagc gtggtgccct cggaccgcgg caactacacc 720
tgcgtcgtgg agaacaagtt tggcagcatc cggcagacgt acacgctgga cgtgctggag 780
cgctccccgc accggcccat cctgcaggcg gggctgccgg ccaaccagac ggcggtgctg 840
ggcagcgacg tggagttcca ctgcaaggtg tacagtgacg cacagcccca catccagtgg 900
ctcaagcacg tggaggtgaa cggcagcaag gtgggcccgg acggcacacc ctacgttacc 960
gtgctcaaga cggcgggcgc taacaccacc gacaaggagc tagaggttct ctccttgcac 1020
aacgtcacct ttgaggacgc cggggagtac acctgcctgg cgggcaattc tattgggttt 1080
tctcatcact ctgcgtggct ggtggtgctg ccagccgagg aggagctggt ggaggctgac 1140
gaggcgggca gtgtgtatgc aggcatcctc agctacgggg tgggcttctt cctgttcatc 1200
ctggtggtgg cggctgtgac gctctgccgc ctgcgcagcc cccccaagaa aggcctgggc 1260
tcccccaccg tgcacaagat ctcccgcttc ccgctcaagc gacaggtgtc cctggagtcc 1320
aacgcgtcca tgagctccaa cacaccactg gtgcgcatcg caaggctgtc ctcaggggag 1380
ggccccacgc tggccaatgt ctccgagctc gagctgcctg ccgaccccaa atgggagctg 1440
tctcgggccc ggctgaccct gggcaagccc cttggggagg gctgcttcgg ccaggtggtc 1500
atggcggagg ccatcggcat tgacaaggac cgggccgcca agcctgtcac cgtagccgtg 1560
aagatgctga aagacgatgc cactgacaag gacctgtcgg acctggtgtc tgagatggag 1620
atgatgaaga tgatcgggaa acacaaaaac atcatcaacc tgctgggcgc ctgcacgcag 1680
ggcgggcccc tgtacgtgct ggtggagtac gcggccaagg gtaacctgcg ggagtttctg 1740
cgggcgcggc ggcccccggg cctggactac tccttcgaca cctgcaagcc gcccgaggag 1800
cagctcacct tcaaggacct ggtgtcctgt gcctaccagg tggcccgggg catggagtac 1860
ttggcctccc agaagtgcat ccacagggac ctggctgccc gcaatgtgct ggtgaccgag 1920
gacaacgtga tgaagatcgc agacttcggg ctggcccggg acgtgcacaa cctcgactac 1980
tacaagaaga caaccaacgg ccggctgccc gtgaagtgga tggcgcctga ggccttgttt 2040
gaccgagtct acactcacca gagtgacgtc tggtcctttg gggtcctgct ctgggagatc 2100
ttcacgctgg ggggctcccc gtaccccggc atccctgtgg aggagctctt caagctgctg 2160
aaggagggcc accgcatgga caagcccgcc aactgcacac acgacctgta catgatcatg 2220
cgggagtgct ggcatgccgc gccctcccag aggcccacct tcaagcagct ggtggaggac 2280
ctggaccgtg tccttaccgt gacgtccacc gacgagtacc tggacctgtc ggcgcctttc 2340
gagcagtact ccccgggtgg ccaggacacc cccagctcca gctcctcagg ggacgactcc 2400
gtgtttgccc acgacctgct gcccccggcc ccacccagca gtgggggctc gcggacgtga 2460
agggccactg gtccccaaca atgtgagggg tccctagcag ccctccctgc tgctggtgca 2520
cagccactcc ccggcatgag actcagtgca gatggagaga cagctacaca gagctttggt 2580
ctgtgtgtgt gtgtgtgcgt gtgtgtgtgt gtgtgcacat ccgcgtgtgc ctgtgtgcgt 2640
gcgcatcttg cctccaggtg cagaggtacc ctgggtgtcc ccgctgctgt gcaacggtct 2700
cctgactggt gctgcagcac cgaggggcct ttgttctggg gggacccagt gcagaatgta 2760
agtgggccca cccggtggga ccccgtgggg cagggagctg ggcccgacat ggctcggcct 2820
ctgcctttgc accacgggac atcacagggt gcgctcggcc cctcccacac ccaaagctga 2880
gcctgcaggg aagccccaca tgtccagcac cttgtgcctg gggtgttagt ggcaccgcct 2940
ccccacctcc aggctttccc acttcccacc ctgcccctca gagactgaaa ttacgggtac 3000

ctgaagatgg gagcctttac cttttatgca aaaggtttat tccggaaact agtgtacatt 3060
tctataaata gatgctgtgt atatggtata tatacatata tatatataac atatatggaa 3120
gaggaaaagg ctggtacaac ggaggcctgc gaccctgggg gcacaggagg caggcatggc 3180
cctgggcggg gcgtgggggg gcgtggaggg aggccccagg ggtctcaccc atgcaagcag 3240
aggaccaggg ctttttctgg caccgcagtt ttgttttaaa actggacctg tatatttgta 3300
aagctattta tgggcccctg gcactcttgt tcccacaccc caacacttcc agcatttagc 3360
tggccacatg gcggagagtt ttaattttta acttattgac aaccgagaag gtttatcccg 3420
ccgatagagg gacggccaag aatgtacgtc cagcctgccc cggagctgga ggatcccctc 3480
caagcctaaa aggttgttaa tagttggagg tgattccagt gaagatattt tatttgcttt 3540
gtccttttc aggagaatta gatttctata ggatttttct ttaggagatt tatttttgg 3600
acttcaaagc aagctggtat tttcatacaa attcttctaa ttgctgtgtg tcccaggcag 3660
ggagacggtt tccagggagg ggccggccct gtgtgcaggt tccgatgtta ttagatgtta 3720
caagtttata tatatctata tatataattt attgagtttt tacaagatgt atttgttgta 3780
gacttaacac ttcttacgca atgcttctag agttttatag cctggactgc tacctttcaa 3840
agcttggagg gaagccgtga attcagttgg ttcgttctgt actgttactg ggccctgagt 3900
ctgggcagct gtcccttgct tgcctgcagg gccatggctc agggtggtct cttcttgggg 3960
cccagtgcat ggtggccaga ggtgtcaccc aaaccggcag gtgcgatttt gttaacccag 4020
cgacgaactt tccgaaaaat aaagacacct ggttgctaac ctgaaaaaaa aaaaaaaaaa 4080
aaaaaaaaaa aaa 4093

<210> 244
<211> 3475
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM004119
<309> 2005-01-22

<400> 244
cgaggcggca tccgagggct gggccggcgc cctgggggac cccgggctcc ggaggccatg 60
ccggcgttgg cgcgcgacgc gggcaccgtg ccgctgctcg ttgtttttc tgcaatgata 120
tttgggacta ttacaaatca agatctgcct gtgatcaagt gtgttttaat caatcataag 180
aacaatgatt catcagtggg gaagtcatca tcatatccca tggtatcaga atccccggaa 240
gacctcgggt gtgcgttgag accccagagc tcagggacag tgtacgaagc tgccgctgtg 300
gaagtggatg tatctgcttc catcacactg caagtgctgg tcgatgcccc agggaacatt 360
tcctgtctct gggtctttaa gcacagctcc ctgaattgcc agccacattt tgatttacaa 420
aacagaggag ttgtttccat ggtcattttg aaaatgacag aaacccaagc tggagaatac 480
ctacttttta ttcagagtga agctaccaat tacacaatat tgtttacagt gagtataaga 540
aataccctgc tttacacatt aagaagacct tactttagaa aaatggaaaa ccaggacgcc 600
ctggtctgca tatctgagag cgttccagag ccgatcgtgg aatgggtgct ttgcgattca 660
caggggaaa gctgtaaaga agaaagtcca gctgttgtta aaaaggagga aaaagtgctt 720
catgaattat ttgggacgga cataaggtgc tgtgccagaa atgaactggg cagggaatgc 780
accaggctgt tcacaataga tctaaatcaa actcctcaga ccacattgcc acaattattt 840
cttaaagtag gggaaccctt atggataagg tgcaaagctg ttcatgtgaa ccatggattc 900
gggctcacct gggaattaga aaacaaagca ctcgaggagg gcaactactt tgagatgagt 960
acctattcaa caaacagaac tatgatacgg attctgtttg cttttgtatc atcagtggca 1020
agaaacgaca ccggatacta cacttgttcc tcttcaaagc atcccagtca atcagctttg 1080
gttaccatcg taggaaaggg atttataaat gctaccaatt caagtgaaga ttatgaaatt 1140
gaccaatatg aagagttttg tttttctgtc aggtttaaag cctacccaca aatcagatgt 1200
acgtggacct tctctcgaaa atcatttcct tgtgagcaaa agggtcttga taacggatac 1260
agcatatcca agttttgcaa tcataagcac cagccaggag aatatatatt ccatgcagaa 1320
aatgatgatg cccaatttac caaaatgttc acgctgaata taagaaggaa acctcaagtg 1380
ctcgcagaag catcggcaag tcaggcgtcc tgtttctcgg atggataccc attaccatct 1440
tggacctgga agaagtgttc agacaagtct cccaactgca cagaagagat cacagaagga 1500
gtctggaata gaaaggctaa cagaaaagtg tttggacagt gggtgtcgag cagtactcta 1560

aacatgagtg aagccataaa agggttcctg gtcaagtgct gtgcatacaa ttcccttggc 1620
acatcttgtg agacgatcct tttaaactct ccaggcccct tccctttcat ccaagacaac 1680
atctcattct atgcaacaat tggtgtttgt ctcctcttca ttgtcgtttt aaccctgcta 1740
atttgtcaca agtacaaaaa gcaatttagg tatgaaagcc agctacagat ggtacaggtg 1800
accggctcct cagataatga gtacttctac gttgatttca gagaatatga atatgatctc 1860
aaatgggagt ttccaagaga aaatttagag tttgggaagg tactaggatc aggtgctttt 1920
ggaaaagtga tgaacgcaac agcttatgga attagcaaaa caggagtctc aatccaggtt 1980
gccgtcaaaa tgctgaaaga aaaagcagac agctctgaaa gagaggcact catgtcagaa 2040
ctcaagatga tgacccagct gggaagccac gagaatattg tgaacctgct gggggcgtgc 2100
acactgtcag gaccaattta cttgattttt gaatactgtt gctatggtga tcttctcaac 2160
tatctaagaa gtaaaagaga aaaatttcac aggacttgga cagagatttt caaggaacac 2220
aatttcagtt tttaccccac tttccaatca catccaaatt ccagcatgcc tggttcaaga 2280
gaagttcaga tacacccgga ctcggatcaa atctcagggc ttcatgggaa ttcatttcac 2340
tctgaagatg aaattgaata tgaaaaccaa aaaaggctgg aagaagagga ggacttgaat 2400
gtgcttacat ttgaagatct tctttgcttt gcatatcaag ttgccaaagg aatggaattt 2460
ctggaattta agtcgtgtgt tcacagagac ctggccgcca ggaacgtgct tgtcacccac 2520
gggaaagtgg tgaagatatg tgactttgga ttggctcgag atatcatgag tgattccaac 2580
tatgttgtca ggggcaatgc ccgtctgcct gtaaaatgga tggcccccga aagcctgttt 2640
gaaggcatct acaccattaa gagtgatgtc tggtcatatg gaatattact gtgggaaatc 2700
ttctcacttg gtgtgaatcc ttaccctggc attccggttg atgctaactt ctacaaactg 2760
attcaaaatg gatttaaaat ggatcagcca ttttatgcta cagaagaaat atacattata 2820
atgcaatcct gctgggcttt tgactcaagg aaacggccat ccttccctaa tttgacttcg 2880
tttttaggat gtcagctggc agatgcagaa gaagcgatgt atcagaatgt ggatggccgt 2940
gtttcggaat gtcctcacac ctaccaaaac aggcgacctt tcagcagaga gatggatttg 3000
gggctactct ctccgcaggc tcaggtcgaa gattcgtaga ggaacaattt agttttaagg 3060
acttcatccc tccacctatc cctaacaggc tgtagattac caaaacaaga ttaatttcat 3120
cactaaaaga aaatctatta tcaactgctg cttcaccaga cttttctcta gaagccgtct 3180
gcgtttactc ttgttttcaa agggactttt gtaaaatcaa atcatcctgt cacaaggcag 3240
gaggagctga taatgaactt tattggagca ttgatctgca tccaaggcct tctcaggccg 3300
gcttgagtga attgtgtacc tgaagtacag tatattcttg taaatacata aaacaaaagc 3360
attttgctaa ggagaagcta atatgatttt ttaagtctat gttttaaaat aatatgtaaa 3420
tttttcagct atttagtgat atattttatg ggtgggaata aaatttctac tacag 3475

<210> 245
<211> 6641
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM000245
<309> 2004-10-28

<400> 245
gccctcgccg cccgcggcgc cccgagcgct ttgtgagcag atgcggagcc gagtggaggg 60
cgcgagccag atgcggggcg acagctgact tgctgagagg aggcggggag gcgcggagcg 120
cgcgtgtggt ccttgcgccg ctgacttctc cactggttcc tgggcaccga aagataaacc 180
tctcataatg aaggcccccg ctgtgcttgc acctggcatc ctcgtgctcc tgtttacctt 240
ggtgcagagg agcaatgggg agtgtaaaga ggcactagca aagtccgaga tgaatgtgaa 300
tatgaagtat cagcttccca acttcaccgc ggaaacaccc atccagaatg tcattctaca 360
tgagcatcac attttccttg gtgccactaa ctacatttat gttttaaatg aggaagacct 420
tcagaaggtt gctgagtaca agactgggcc tgtgctggaa cacccagatt gtttcccatg 480
tcaggactgc agcagcaaag ccaatttatc aggaggtgtt tggaaagata acatcaacat 540
ggctctagtt gtcgacacct actatgatga tcaactcatt agctgtggca gcgtcaacag 600
agggacctgc cagcgacatg tctttcccca caatcatact gctgacatac agtcggaggt 660
tcactgcata ttctccccac agatagaaga gcccagccag tgtcctgact gtgtggtgag 720
cgccctggga gccaaagtcc tttcatctgt aaaggaccgg ttcatcaact tctttgtagg 780

caataccata aattcttctt atttcccaga tcatccattg cattcgatat cagtgagaag 840
gctaaaggaa acgaaagatg gttttatgtt tttgacggac cagtcctaca ttgatgtttt 900
acctgagttc agagattctt accccattaa gtatgtccat gcctttgaaa gcaacaattt 960
tatttacttc ttgacggtcc aaagggaaac tctagatgct cagacttttc acacaagaat 1020
aatcaggttc tgttccataa actctggatt gcattcctac atggaaatgc ctctggagtg 1080
tattctcaca gaaaagagaa aaaagagatc cacaaagaag gaagtgttta atatacttca 1140
ggctgcgtat gtcagcaagc ctggggccca gcttgctaga caaataggag ccagcctgaa 1200
tgatgacatt cttttcgggg tgttcgcaca aagcaagcca gattctgccg aaccaatgga 1260
tcgatctgcc atgtgtgcat tccctatcaa atatgtcaac gacttcttca acaagatcgt 1320
caacaaaaac aatgtgagat gtctccagca tttttacgga cccaatcatg agcactgctt 1380
taataggaca cttctgagaa attcatcagg ctgtgaagcg cgccgtgatg aatatcgaac 1440
agagtttacc acagctttgc agcgcgttga cttattcatg ggtcaattca gcgaagtcct 1500
cttaacatct atatccacct tcattaaagg agacctcacc atagctaatc ttgggacatc 1560
agagggtcgc ttcatgcagg ttgtggtttc tcgatcagga ccatcaaccc ctcatgtgaa 1620
ttttctcctg gactcccatc cagtgtctcc agaagtgatt gtggagcata cattaaacca 1680
aaatggctac acactggtta tcactgggaa gaagatcacg aagatcccat tgaatggctt 1740
gggctgcaga catttccagt cctgcagtca atgcctctct gccccaccct ttgttcagtg 1800
tggctggtgc cacgacaaat gtgtgcgatc ggaggaatgc ctgagcggga catggactca 1860
acagatctgt ctgcctgcaa tctacaaggt tttcccaaat agtgcacccc ttgaaggagg 1920
gacaaggctg accatatgtg gctgggactt tggatttcgg aggaataata aatttgattt 1980
aaagaaaact agagttctcc ttggaaatga gagctgcacc ttgactttaa gtgagagcac 2040
gatgaataca ttgaaatgca cagttggtcc tgccatgaat aagcatttca atatgtccat 2100
aattatttca aatggccacg ggacaacaca atacagtaca ttctcctatg tggatcctgt 2160
aataacaagt atttcgccga aatacggtcc tatggctggt ggcactttac ttactttaac 2220
tggaaattac ctaaacagtg ggaattctag acacatttca attggtggaa aaacatgtac 2280
tttaaaaagt gtgtcaaaca gtattcttga atgttatacc ccagcccaaa ccatttcaac 2340
tgagtttgct gttaaattga aaattgactt agccaaccga gagacaagca tcttcagtta 2400
ccgtgaagat cccattgtct atgaaattca tccaaccaaa tcttttatta gtggtgggag 2460
cacaataaca ggtgttggga aaaacctgaa ttcagttagt gtcccgagaa tggtcataaa 2520
tgtgcatgaa gcaggaagga actttacagt ggcatgtcaa catcgctcta attcagagat 2580
aatctgttgt accactcctt ccctgcaaca gctgaatctg caactccccc tgaaaaccaa 2640
agccttttc atgttagatg ggatcctttc caaatacttt gatctcattt atgtacataa 2700
tcctgtgttt aagccttttg aaaagccagt gatgatctca atgggcaatg aaaatgtact 2760
ggaaattaag ggaaatgata ttgaccctga agcagttaaa ggtgaagtgt taaaagttgg 2820
aaataagagc tgtgagaata tacacttaca ttctgaagcc gttttatgca cggtccccaa 2880
tgacctgctg aaattgaaca gcgagctaaa tatagagtgg aagcaagcaa tttcttcaac 2940
cgtccttgga aaagtaatag ttcaaccaga tcagaatttc acaggattga ttgctggtgt 3000
tgtctcaata tcaacagcac tgttattact acttgggttt ttcctgtggc tgaaaaagag 3060
aaagcaaatt aaagatctgg gcagtgaatt agttcgctac gatgcaagag tacacactcc 3120
tcatttggat aggcttgtaa gtgcccgaag tgtaagccca actacagaaa tggtttcaaa 3180
tgaatctgta gactaccgag ctacttttcc agaagatcag tttcctaatt catctcagaa 3240
cggttcatgc cgacaagtgc agtatcctct gacagacatg tcccccatcc taactagtgg 3300
ggactctgat atatccagtc cattactgca aaatactgtc cacattgacc tcagtgctct 3360
aaatccagag ctggtccagg cagtgcagca tgtagtgatt gggcccagta gcctgattgt 3420
gcatttcaat gaagtcatag gaagagggca ttttggttgt gtatatcatg ggactttgtt 3480
ggacaatgat ggcaagaaaa ttcactgtgc tgtgaaatcc ttgaacagaa tcactgacat 3540
aggagaagtt tcccaatttc tgaccgaggg aatcatcatg aaagatttta gtcatcccaa 3600
tgtcctctcg ctcctgggaa tctgcctgcg aagtgaaggg tctccgctgg tggtcctacc 3660
atacatgaaa catggagatc ttcgaaattt cattcgaaat gagactcata atccaactgt 3720
aaaagatctt attggctttg gtcttcaagt agccaaaggc atgaaatatc ttgcaagcaa 3780
aaagtttgtc cacagagact tggctgcaag aaactgtatg ctggatgaaa aattcacagt 3840
caaggttgct gattttggtc ttgccagaga catgtatgat aaagaatact atagtgtaca 3900
caacaaaaca ggtgcaaagc tgccagtgaa gtggatggct ttggaaagtc tgcaaactca 3960
aaagtttacc accaagtcag atgtgtggtc ctttggcgtg ctcctctggg agctgatgac 4020
aagaggagcc ccaccttatc ctgacgtaaa caccttgat ataactgttt acttgttgca 4080
agggagaaga ctcctacaac ccgaatactg cccagacccc ttatatgaag taatgctaaa 4140

atgctggcac cctaaagccg aaatgcgccc atccttttct gaactggtgt cccggatatc 4200
agcgatcttc tctactttca ttggggagca ctatgtccat gtgaacgcta cttatgtgaa 4260
cgtaaaatgt gtcgctccgt atccttctct gttgtcatca gaagataacg ctgatgatga 4320
ggtggacaca cgaccagcct ccttctggga gacatcatag tgctagtact atgtcaaagc 4380
aacagtccac actttgtcca atggtttttt cactgcctga cctttaaaag gccatcgata 4440
ttctttgctc ttgccaaaat tgcactatta taggacttgt attgttattt aaattactgg 4500
attctaagga atttcttatc tgacagagca tcagaaccag aggcttggtc ccacaggcca 4560
cggaccaatg gcctgcagcc gtgacaacac tcctgtcata ttggagtcca aaacttgaat 4620
tctgggttga atttttaaa aatcaggtac cacttgattt catatgggaa attgaagcag 4680
gaaatattga gggcttcttg atcacagaaa actcagaaga gatagtaatg ctcaggacag 4740
gagcggcagc cccagaacag gccactcatt tagaattcta gtgtttcaaa acacttttgt 4800
gtgttgtatg gtcaataaca tttttcatta ctgatggtgt cattcaccca ttaggtaaac 4860
attccctttt aaatgtttgt ttgttttttg agacaggatc tcactctgtt gccagggctg 4920
tagtgcagtg gtgtgatcat agctcactgc aacctccacc tcccaggctc aagcctcccg 4980
aatagctggg actacaggcg cacaccacca tccccggcta atttttgtat tttttgtaga 5040
gacggggttt tgccatgttg ccaaggctgg tttcaaactc ctggactcaa gaaatccacc 5100
cacctcagcc tcccaaagtg ctaggattac aggcatgagc cactgcgccc agcccttata 5160
aatttttgta tagacattcc tttggttgga agaatattta taggcaatac agtcaaagtt 5220
tcaaaatagc atcacacaaa acatgtttat aaatgaacag gatgtaatgt acatagatga 5280
cattaagaaa atttgtatga aataatttag tcatcatgaa atatttagtt gtcatataaa 5340
aacccactgt ttgagaatga tgctactctg atctaatgaa tgtgaacatg tagatgtttt 5400
gtgtgtattt ttttaaatga aaactcaaaa taagacaagt aatttgttga taaatatttt 5460
taaagataac tcagcatgtt tgtaaagcag gatacatttt actaaaaggt tcattggttc 5520
caatcacagc tcataggtag agcaaagaaa gggtggatgg attgaaaaga ttagcctctg 5580
tctcggtggc aggttcccac ctcgcaagca attggaaaca aaacttttgg ggagttttat 5640
tttgcattag ggtgtgtttt atgttaagca aaacatactt tagaaacaaa tgaaaaaggc 5700
aattgaaaat cccagctatt tcacctagat ggaatagcca ccctgagcag aactttgtga 5760
tgcttcattc tgtggaattt tgtgcttgct actgtatagt gcatgtggtg taggttactc 5820
taactggttt tgtcgacgta aacatttaaa gtgttatatt ttttataaaa atgtttattt 5880
ttaatgatat gagaaaaatt ttgttaggcc acaaaaacac tgcactgtga acattttaga 5940
aaaggtatgt cagactggga ttaatgacag catgattttc aatgactgta aattgcgata 6000
aggaaatgta ctgattgcca atacacccca ccctcattac atcatcagga cttgaagcca 6060
agggttaacc cagcaagcta caaagagggt gtgtcacact gaaactcaat agttgagttt 6120
ggctgttgtt gcaggaaaat gattataact aaaagctctc tgatagtgca gagacttacc 6180
agaagacaca aggaattgta ctgaagagct attacaatcc aaatattgcc gtttcataaa 6240
tgtaataagt aatactaatt cacagagtat tgtaaatggt ggatgacaaa agaaaatctg 6300
ctctgtggaa agaaagaact gtctctacca gggtcaagag catgaacgca tcaatagaaa 6360
gaactcgggg aaacatccca tcaacaggac tacacacttg tatatacatt cttgagaaca 6420
ctgcaatgtg aaaatcacgt ttgctattta taaacttgtc cttagattaa tgtgtctgga 6480
cagattgtgg gagtaagtga ttcttctaag aattagatac ttgtcactgc ctatacctgc 6540
agctgaactg aatggtactt cgtatgttaa tagttgttct gataaatcat gcaattaaag 6600
taaagtgatg caacatcttg taaaaaaaaa aaaaaaaaaa a 6641

<210> 246
<211> 6633
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM006206
<309> 2004-10-26

<400> 246
ttctccccgc cccccagttg ttgtcgaagt ctgggggttg ggactggacc ccctgattgc 60

gtaagagcaa aaagcgaagg cgcaatctgg acactgggag attcggagcg cagggagttt 120
gagagaaact tttattttga agagaccaag gttgaggggg ggcttatttc ctgacagcta 180
tttacttaga gcaaatgatt agttttagaa ggatggacta taacattgaa tcaattacaa 240
aacgcggttt ttgagcccat tactgttgga gctacaggga gagaaacagg aggagactgc 300
aagagatcat ttgggaaggc cgtgggcacg ctctttactc catgtgtggg acattcattg 360
cggaataaca tcggaggaga agtttcccag agctatgggg acttcccatc cggcgttcct 420
ggtcttaggc tgtcttctca cagggctgag cctaatcctc tgccagcttt cattaccctc 480
tatccttcca aatgaaaatg aaaaggttgt gcagctgaat tcatcctttt ctctgagatg 540
ctttggggag agtgaagtga gctggcagta ccccatgtct gaagaagaga gctccgatgt 600
ggaaatcaga aatgaagaaa acaacagcgg ccttttgtg acggtcttgg aagtgagcag 660
tgcctcggcg gcccacacag ggttgtacac ttgctattac aaccacactc agacagaaga 720
gaatgagctt gaaggcaggc acatttacat ctatgtgcca gacccagatg tagcctttgt 780
acctctagga atgacggatt atttagtcat cgtggaggat gatgattctg ccattatacc 840
ttgtcgcaca actgatcccg agactcctgt aaccttacac aacagtgagg gggtggtacc 900
tgcctcctac gacagcagac agggctttaa tgggaccttc actgtagggc cctatatctg 960
tgaggccacc gtcaaaggaa agaagttcca gaccatccca tttaatgttt atgctttaaa 1020
agcaacatca gagctggatc tagaaatgga agctcttaaa accgtgtata agtcagggga 1080
aacgattgtg gtcacctgtg ctgtttttaa caatgaggtg gttgaccttc aatggactta 1140
ccctggagaa gtgaaaggca aaggcatcac aatgctggaa gaaatcaaag tcccatccat 1200
caaattggtg tacactttga cggtccccga ggccacggtg aaagacagtg gagattacga 1260
atgtgctgcc cgccaggcta ccagggaggt caaagaaatg aagaaagtca ctatttctgt 1320
ccatgagaaa ggtttcattg aaatcaaacc caccttcagc cagttggaag ctgtcaacct 1380
gcatgaagtc aaacattttg ttgtagaggt gcgggcctac ccacctccca ggatatcctg 1440
gctgaaaaac aatctgactc tgattgaaaa tctcactgag atcaccactg atgtggaaaa 1500
gattcaggaa ataaggtatc gaagcaaatt aaagctgatc cgtgctaagg aagaagacag 1560
tggccattat actattgtag ctcaaaatga agatgctgtg aagagctata cttttgaact 1620
gttaactcaa gttccttcat ccattctgga cttggtcgat gatcaccatg gctcaactgg 1680
gggacagacg gtgaggtgca cagctgaagg cacgccgctt cctgatattg agtggatgat 1740
atgcaaagat attaagaaat gtaataatga aacttcctgg actattttgg ccaacaatgt 1800
ctcaaacatc atcacggaga tccactcccg agacaggagt accgtggagg gccgtgtgac 1860
tttcgccaaa gtggaggaga ccatcgccgt gcgatgcctg gctaagaatc tccttggagc 1920
tgagaaccga gagctgaagc tggtggctcc caccctgcgt tctgaactca cggtggctgc 1980
tgcagtcctg gtgctgttgg tgattgtgat catctcactt attgtcctgg ttgtcatttg 2040
gaaacagaaa ccgaggtatg aaattcgctg gagggtcatt gaatcaatca gcccggatgg 2100
acatgaatat atttatgtgg acccgatgca gctgccttat gactcaagat gggagtttcc 2160
aagagatgga ctagtgcttg gtcgggtctt ggggtctgga gcgtttggga aggtggttga 2220
aggaacagcc tatggattaa gccggtccca acctgtcatg aaagttgcag tgaagatgct 2280
aaaacccacg gccagatcca gtgaaaaaca agctctcatg tctgaactga agataatgac 2340
tcacctgggg ccacatttga acattgtaaa cttgctggga gcctgcacca agtcaggccc 2400
catttacatc atcacagagt attgcttcta tggagatttg gtcaactatt tgcataagaa 2460
tagggatagc ttcctgagcc accacccaga gaagccaaag aaagagctgg atatctttgg 2520
attgaaccct gctgatgaaa gcacacggag ctatgttatt ttatcttttg aaaacaatgg 2580
tgactacatg gacatgaagc aggctgatac tacacagtat gtccccatgc tagaaaggaa 2640
agaggtttct aaatattccg acatccagag atcactctat gatcgtccag cctcatataa 2700
gaagaaatct atgttagact cagaagtcaa aaacctcctt tcagatgata actcagaagg 2760
ccttacttta ttggatttgt tgagcttcac ctatcaagtt gcccgaggaa tggagttttt 2820
ggcttcaaaa aattgtgtcc accgtgatct ggctgctcgc aacgtcctcc tggcacaagg 2880
aaaaattgtg aagatctgtg actttggcct ggccagagac atcatgcatg attcgaacta 2940
tgtgtcgaaa ggcagtacct ttctgcccgt gaagtggatg gctcctgaga gcatctttga 3000
caacctctac accacactga gtgatgtctg gtcttatggc attctgctct gggagatctt 3060
ttcccttggt ggcacccctt accccggcat gatggtggat tctactttct acaataagat 3120
caagagtggg taccggatgg ccaagcctga ccacgctacc agtgaagtct acgagatcat 3180
ggtgaaatgc tggaacagtg agccggagaa gagaccctcc ttttaccacc tgagtgagat 3240
tgtggagaat ctgctgcctg gacaatataa aaagagttat gaaaaaattc acctggactt 3300
cctgaagagt gaccatcctg ctgtggcacg catgcgtgtg gactcagaca atgcatacat 3360
tggtgtcacc tacaaaaacg aggaagacaa gctgaaggac tgggagggtg gtctggatga 3420

gcagagactg agcgctgaca gtggctacat cattcctctg cctgacattg accctgtccc 3480
tgaggaggag gacctgggca agaggaacag acacagctcg cagacctctg aagagagtgc 3540
cattgagacg ggttccagca gttccacctt catcaagaga gaggacgaga ccattgaaga 3600
catcgacatg atggacgaca tcggcataga ctcttcagac ctggtggaag acagcttcct 3660
gtaactggcg gattcgaggg gttccttcca cttctggggc cacctctgga tcccgttcag 3720
aaaaccactt tattgcaatg cggaggttga gaggaggact tggttgatgt ttaaagagaa 3780
gttcccagcc aagggcctcg gggagcgttc taaatatgaa tgaatgggat attttgaaat 3840
gaactttgtc agtgttgcct ctcgcaatgc ctcagtagca tctcagtggt gtgtgaagtt 3900
tggagataga tggataaggg aataataggc cacagaaggt gaactttgtg cttcaaggac 3960
attggtgaga gtccaacaga cacaatttat actgcgacag aacttcagca ttgtaattat 4020
gtaaataact ctaaccaagg ctgtgtttag attgtattaa ctatcttctt tggacttctg 4080
aagagaccac tcaatccatc catgtacttc cctcttgaaa cctgatgtca gctgctgttg 4140
aacttttaa agaagtgcat gaaaaaccat ttttgaacct taaaaggtac tggtactata 4200
gcattttgct atcttttta gtgttaagag ataaagaata ataattaacc aaccttgttt 4260
aatagatttg ggtcatttag aagcctgaca actcattttc atattgtaat ctatgtttat 4320
aatactacta ctgttatcag taatgctaaa tgtgtaataa tgtaacatga tttccctcca 4380
gagaaagcac aatttaaaac aatccttact aagtaggtga tgagtttgac agtttttgac 4440
atttatatta aataacatgt ttctctataa agtatggtaa tagctttagt gaattaaatt 4500
tagttgagca tagagaacaa agtaaaagta gtgttgtcca ggaagtcaga atttttaact 4560
gtactgaata ggttccccaa tccatcgtat taaaaaacaa ttaactgccc tctgaaataa 4620
tgggattaga aacaaacaaa actcttaagt cctaaaagtt ctcaatgtag aggcataaac 4680
ctgtgctgaa cataacttct catgtatatt acccaatgga aaatataatg atcagcaaaa 4740
agactggatt tgcagaagtt ttttttttt ttcttcatgc ctgatgaaag ctttggcaac 4800
cccaatatat gtatttttg aatctatgaa cctgaaaagg gtcagaagga tgcccagaca 4860
tcagcctcct tctttcaccc cttaccccaa agagaaagag tttgaaactc gagaccataa 4920
agatattctt tagtggaggc tggatgtgca ttagcctgga tcctcagttc tcaaatgtgt 4980
gtggcagcca ggatgactag atcctgggtt tccatccttg agattctgaa gtatgaagtc 5040
tgagggaaac cagagtctgt atttttctaa actccctggc tgttctgatc ggccagtttt 5100
cggaaacact gacttaggtt tcaggaagtt gccatgggaa acaaataatt tgaactttgg 5160
aacagggttg gaattcaacc acgcaggaag cctactattt aaatccttgg cttcaggtta 5220
gtgacattta atgccatcta gctagcaatt gcgaccttaa tttaactttc cagtcttagc 5280
tgaggctgag aaagctaaag tttggttttg acaggttttc caaaagtaaa gatgctactt 5340
cccactgtat gggggagatt gaactttccc cgtctcccgt cttctgcctc ccactccata 5400
ccccgccaag gaaaggcatg tacaaaaatt atgcaattca gtgttccaag tctctgtgta 5460
accagctcag tgttttggtg gaaaaaacat tttaagtttt actgataatt tgaggttaga 5520
tgggaggatg aattgtcaca tctatccaca ctgtcaaaca ggttggtgtg ggttcattgg 5580
cattctttgc aatactgctt aattgctgat accatatgaa tgaaacatgg gctgtgatta 5640
ctgcaatcac tgtgctatcg gcagatgatg ctttggaaga tgcagaagca ataataaagt 5700
acttgactac ctactggtgt aatctcaatg caagccccaa ctttcttatc caacttttc 5760
atagtaagtg cgaagactga gccagattgg ccaattaaaa acgaaaacct gactaggttc 5820
tgtagagcca attagacttg aaatacgttt gtgtttctag aatcacagct caagcattct 5880
gtttatcgct cactctccct tgtacagcct tattttgttg gtgctttgca ttttgatatt 5940
gctgtgagcc ttgcatgaca tcatgaggcc ggatgaaact tctcagtcca gcagtttcca 6000
gtcctaacaa atgctcccac ctgaatttgt atatgactgc atttgtgggt gtgtgtgtgt 6060
tttcagcaaa ttccagattt gtttcctttt ggcctcctgc aaagtctcca gaagaaaatt 6120
tgccaatctt tcctactttc tatttttatg atgacaatca aagccggcct gagaaacact 6180
atttgtgact ttttaaacga ttagtgatgt ccttaaaatg tggtctgcca atctgtacaa 6240
aatggtccta tttttgtgaa gagggacata agataaaatg atgttataca tcaatatgta 6300
tatatgtatt tctatataga cttggagaat actgccaaaa catttatgac aagctgtatc 6360
actgccttcg tttatatttt tttaactgtg ataatcccca caggcacatt aactgttgca 6420
cttttgaatg tccaaaattt atattttaga aataataaaa agaaagatac ttacatgttc 6480
ccaaaacaat ggtgtggtga atgtgtgaga aaaactaact tgatagggtc taccaataca 6540
aaatgtatta cgaatgcccc tgttcatgtt tttgttttaa aacgtgtaaa tgaagatctt 6600
tatatttcaa taaatgatat ataatttaaa gtt 6633

<210> 247
<211> 2236
<212> DNA
<213> Homo sapiens

<300>
<308> GenBank No. NM001065
<309> 2004-10-27

<400> 247
gctgttgcaa cactgcctca ctcttcccct cccaccttct ctcccctcct ctctgcttta 60
attttctcag aattctctgg actgaggctc cagttctggc ctttggggtt caagatcact 120
gggaccaggc cgtgatctct atgcccgagt ctcaaccctc aactgtcacc ccaaggcact 180
tgggacgtcc tggacagacc gagtcccggg aagccccagc actgccgctg ccacactgcc 240
ctgagcccaa atgggggagt gagaggccat agctgtctgg catgggcctc tccaccgtgc 300
ctgacctgct gctgccactg gtgctcctgg agctgttggt gggaatatac ccctcagggg 360
ttattggact ggtccctcac ctaggggaca gggagaagag agatagtgtg tgtccccaag 420
gaaaatatat ccaccctcaa aataattcga tttgctgtac caagtgccac aaaggaacct 480
acttgtacaa tgactgtcca ggcccggggc aggatacgga ctgcagggag tgtgagagcg 540
gctccttcac cgcttcagaa aaccacctca gacactgcct cagctgctcc aaatgccgaa 600
aggaaatggg tcaggtggag atctcttctt gcacagtgga ccgggacacc gtgtgtggct 660
gcaggaagaa ccagtaccgg cattattgga gtgaaaacct tttccagtgc ttcaattgca 720
gcctctgcct caatgggacc gtgcacctct cctgccagga gaaacagaac accgtgtgca 780
cctgccatgc aggtttcttt ctaagagaaa acgagtgtgt ctcctgtagt aactgtaaga 840
aaagcctgga gtgcacgaag ttgtgcctac cccagattga gaatgttaag ggcactgagg 900
actcaggcac cacagtgctg ttgcccctgg tcattttctt tggtctttgc cttttatccc 960
tcctcttcat tggtttaatg tatcgctacc aacggtggaa gtccaagctc tactccattg 1020
tttgtgggaa atcgacacct gaaaaagagg gggagcttga aggaactact actaagcccc 1080
tggccccaaa cccaagcttc agtcccactc caggcttcac ccccaccctg ggcttcagtc 1140
ccgtgcccag ttccaccttc acctccagct ccacctatac ccccggtgac tgtcccaact 1200
ttgcggctcc ccgcagagag gtggcaccac cctatcaggg ggctgacccc atccttgcga 1260
cagccctcgc ctccgacccc atccccaacc cccttcagaa gtgggaggac agcgcccaca 1320
agccacagag cctagacact gatgaccccg cgacgctgta cgccgtggtg gagaacgtgc 1380
ccccgttgcg ctggaaggaa ttcgtgcggc gcctagggct gagcgaccac gagatcgatc 1440
ggctggagct gcagaacggg cgctgcctgc gcgaggcgca atacagcatg ctggcgacct 1500
ggaggcggcg cacgccgcgg cgcgaggcca cgctggagct gctgggacgc gtgctccgcg 1560
acatggacct gctgggctgc ctggaggaca tcgaggaggc gctttgcggc cccgccgccc 1620
tcccgcccgc gcccagtctt ctcagatgag gctgcgcccc tgcgggcagc tctaaggacc 1680
gtcctgcgag atcgccttcc aaccccactt ttttctggaa aggaggggtc ctgcaggggc 1740
aagcaggagc tagcagccgc ctacttggtg ctaacccctc gatgtacata gcttttctca 1800
gctgcctgcg cgccgccgac agtcagcgct gtgcgcgcgg agagaggtgc gccgtgggct 1860
caagagcctg agtgggtggt ttgcgaggat gagggacgct atgcctcatg cccgttttgg 1920
gtgtcctcac cagcaaggct gctcgggggc ccctggttcg tccctgagcc tttttcacag 1980
tgcataagca gttttttttg tttttgtttt gttttgtttt gtttttaaat caatcatgtt 2040
acactaatag aaacttggca ctcctgtgcc ctctgcctgg acaagcacat agcaagctga 2100
actgtcctaa ggcaggggcg agcacggaac aatggggcct tcagctggag ctgtggactt 2160
ttgtacatac actaaaattc tgaagttaaa gctctgctct tggaaaaaaa aaaaaaaaaa 2220
aaaaaaaaaa aaaaaa 2236

<210> 248
<211> 5830
<212> DNA
<213> Homo sapiens

<300>

<308> GenBank No. NM002253
<309> 2004-10-26

<400> 248
actgagtccc gggaccccgg gagagcggtc agtgtgtggt cgctgcgttt cctctgcctg 60
cgccgggcat cacttgcgcg ccgcagaaag tccgtctggc agcctggata tcctctccta 120
ccggcacccg cagacgcccc tgcagccgcc ggtcggcgcc cgggctccct agccctgtgc 180
gctcaactgt cctgcgctgc ggggtgccgc gagttccacc tccgcgcctc cttctctaga 240
caggcgctgg gagaaagaac cggctcccga gttctgggca tttcgcccgg ctcgaggtgc 300
aggatgcaga gcaaggtgct gctggccgtc gccctgtggc tctgcgtgga gacccgggcc 360
gcctctgtgg gtttgcctag tgtttctctt gatctgccca ggctcagcat acaaaaagac 420
atacttacaa ttaaggctaa tacaactctt caaattactt gcaggggaca gagggacttg 480
gactggcttt ggcccaataa tcagagtggc agtgagcaaa gggtggaggt gactgagtgc 540
agcgatggcc tcttctgtaa gacactcaca attccaaaag tgatcggaaa tgacactgga 600
gcctacaagt gcttctaccg ggaaactgac ttggcctcgg tcatttatgt ctatgttcaa 660
gattacagat ctccatttat tgcttctgtt agtgaccaac atggagtcgt gtacattact 720
gagaacaaaa acaaaactgt ggtgattcca tgtctcgggt ccatttcaaa tctcaacgtg 780
tcactttgtg caagataccc agaaaagaga tttgttcctg atggtaacag aatttcctgg 840
gacagcaaga agggctttac tattcccagc tacatgatca gctatgctgg catggtcttc 900
tgtgaagcaa aaattaatga tgaaagttac cagtctatta tgtacatagt tgtcgttgta 960
gggtatagga tttatgatgt ggttctgagt ccgtctcatg gaattgaact atctgttgga 1020
gaaaagcttg tcttaaattg tacagcaaga actgaactaa atgtggggat tgacttcaac 1080
tgggaatacc cttcttcgaa gcatcagcat aagaaacttg taaaccgaga cctaaaaacc 1140
cagtctggga gtgagatgaa gaaatttttg agcaccttaa ctatagatgg tgtaacccgg 1200
agtgaccaag gattgtacac ctgtgcagca tccagtgggc tgatgaccaa gaagaacagc 1260
acatttgtca gggtccatga aaaacctttt gttgcttttg gaagtggcat ggaatctctg 1320
gtggaagcca cggtggggga gcgtgtcaga atccctgcga agtaccttgg ttacccaccc 1380
ccagaaataa aatggtataa aaatggaata ccccttgagt ccaatcacac aattaaagcg 1440
gggcatgtac tgacgattat ggaagtgagt gaaagagaca caggaaatta cactgtcatc 1500
cttaccaatc ccatttcaaa ggagaagcag agccatgtgg tctctctggt tgtgtatgtc 1560
ccaccccaga ttggtgagaa atctctaatc tctcctgtgg attcctacca gtacggcacc 1620
actcaaacgc tgacatgtac ggtctatgcc attcctcccc cgcatcacat ccactggtat 1680
tggcagttgg aggaagagtg cgccaacgag cccagccaag ctgtctcagt gacaaaccca 1740
taccttgtg aagaatggag aagtgtggag gacttccagg gaggaaataa aattgaagtt 1800
aataaaaatc aatttgctct aattgaagga aaaaacaaaa ctgtaagtac ccttgttatc 1860
caagcggcaa atgtgtcagc tttgtacaaa tgtgaagcgg tcaacaaagt cgggagagga 1920
gagagggtga tctccttcca cgtgaccagg ggtcctgaaa ttactttgca acctgacatg 1980
cagcccactg agcaggagag cgtgtctttg tggtgcactg cagacagatc tacgtttgag 2040
aacctcacat ggtacaagct tggcccacag cctctgccaa tccatgtggg agagttgccc 2100
acacctgttt gcaagaactt ggatactctt tggaaattga atgccaccat gttctctaat 2160
agcacaaatg acattttgat catggagctt aagaatgcat ccttgcagga ccaaggagac 2220
tatgtctgcc ttgctcaaga caggaagacc aagaaaagac attgcgtggt caggcagctc 2280
acagtcctag agcgtgtggc acccacgatc acaggaaacc tggagaatca gacgacaagt 2340
attggggaaa gcatcgaagt ctcatgcacg gcatctggga atccccctcc acagatcatg 2400
tggtttaaag ataatgagac ccttgtagaa gactcaggca ttgtattgaa ggatgggaac 2460
cggaacctca ctatccgcag agtgaggaag gaggacgaag gcctctacac ctgccaggca 2520
tgcagtgttc ttggctgtgc aaaagtggag gcatttttca taatagaagg tgcccaggaa 2580
aagacgaact tggaaatcat tattctagta ggcacggcgg tgattgccat gttcttctgg 2640
ctacttcttg tcatcatcct acggaccgtt aagcgggcca atggagggga actgaagaca 2700
ggctacttgt ccatcgtcat ggatccagat gaactcccat tggatgaaca ttgtgaacga 2760
ctgccttatg atgccagcaa atgggaattc cccagagacc ggctgaagct aggtaagcct 2820
cttggccgtg gtgcctttgg ccaagtgatt gaagcagatg cctttggaat tgacaagaca 2880
gcaacttgca ggacagtagc agtcaaaatg ttgaaagaag gagcaacaca cagtgagcat 2940
cgagctctca tgtctgaact caagatcctc attcatattg gtcaccatct caatgtggtc 3000
aaccttctag gtgcctgtac caagccagga gggccactca tggtgattgt ggaattctgc 3060
aaatttggaa acctgtccac ttacctgagg agcaagagaa atgaatttgt cccctacaag 3120

accaaagggg cacgattccg tcaagggaaa gactacgttg gagcaatccc tgtggatctg 3180
aaacggcgct tggacagcat caccagtagc cagagctcag ccagctctgg atttgtggag 3240
gagaagtccc tcagtgatgt agaagaagag gaagctcctg aagatctgta taaggacttc 3300
ctgaccttgg agcatctcat ctgttacagc ttccaagtgg ctaagggcat ggagttcttg 3360
gcatcgcgaa agtgtatcca cagggacctg gcggcacgaa atatcctctt atcggagaag 3420
aacgtggtta aaatctgtga ctttggcttg gcccgggata tttataaaga tccagattat 3480
gtcagaaaag gagatgctcg cctccctttg aaatggatgg ccccagaaac aatttttgac 3540
agagtgtaca caatccagag tgacgtctgg tcttttggtg ttttgctgtg ggaaatattt 3600
tccttaggtg cttctccata tcctggggta aagattgatg aagaattttg taggcgattg 3660
aaagaaggaa ctagaatgag ggcccctgat tatactacac cagaaatgta ccagaccatg 3720
ctggactgct ggcacgggga gcccagtcag agacccacgt tttcagagtt ggtggaacat 3780
ttgggaaatc tcttgcaagc taatgctcag caggatggca aagactacat tgttcttccg 3840
atatcagaga ctttgagcat ggaagaggat tctggactct ctctgcctac ctcacctgtt 3900
tcctgtatgg aggaggagga agtatgtgac cccaaattcc attatgacaa cacagcagga 3960
atcagtcagt atctgcagaa cagtaagcga aagagccggc ctgtgagtgt aaaaacattt 4020
gaagatatcc cgttagaaga accagaagta aaagtaatcc cagatgacaa ccagacggac 4080
agtggtatgg ttcttgcctc agaagagctg aaaactttgg aagacagaac caaattatct 4140
ccatcttttg gtggaatggt gcccagcaaa agcagggagt ctgtggcatc tgaaggctca 4200
aaccagacaa gcggctacca gtccggatat cactccgatg acacagacac caccgtgtac 4260
tccagtgagg aagcagaact tttaaagctg atagagattg gagtgcaaac cggtagcaca 4320
gcccagattc tccagcctga ctcggggacc acactgagct ctcctcctgt ttaaaaggaa 4380
gcatccacac cccaactccc ggacatcaca tgagaggtct gctcagattt tgaagtgttg 4440
ttctttccac cagcaggaag tagccgcatt tgattttcat ttcgacaaca gaaaaaggac 4500
ctcggactgc agggagccag tcttctaggc atatcctgga agaggcttgt gacccaagaa 4560
tgtgtctgtg tcttctccca gtgttgacct gatcctcttt tttcattcat ttaaaaagca 4620
ttatcatgcc cctgctgcgg gtctcaccat gggtttagaa caaagagctt caagcaatgg 4680
ccccatcctc aaagaagtag cagtacctgg ggagctgaca cttctgtaaa actagaagat 4740
aaaccaggca acgtaagtgt tcgaggtgtt gaagatggga aggatttgca gggctgagtc 4800
tatccaagag gctttgttta ggacgtgggt cccaagccaa gccttaagtg tggaattcgg 4860
attgatagaa aggaagacta acgttacctt gctttggaga gtactggagc ctgcaaatgc 4920
attgtgtttg ctctggtgga ggtgggcatg gggtctgttc tgaaatgtaa agggttcaga 4980
cggggtttct ggttttagaa ggttgcgtgt tcttcgagtt gggctaaagt agagttcgtt 5040
gtgctgtttc tgactcctaa tgagagttcc ttccagaccg ttagctgtct ccttgccaag 5100
ccccaggaag aaaatgatgc agctctggct ccttgtctcc caggctgatc ctttattcag 5160
aataccacaa agaaaggaca ttcagctcaa ggctccctgc cgtgttgaag agttctgact 5220
gcacaaacca gcttctggtt tcttctggaa tgaataccct catatctgtc ctgatgtgat 5280
atgtctgaga ctgaatgcgg gaggttcaat gtgaagctgt gtgtggtgtc aaagtttcag 5340
gaaggatttt acccttttgt tcttcccccc gtccccaacc cactctcacc ccgcaaccca 5400
tcagtatttt agttatttgg cctctactcc agtaaacctg attgggtttg ttcactctct 5460
gaatgattat tagccagact tcaaaattat tttatagccc aaattataac atctattgta 5520
ttatttagac ttttaacata tagagctatt tctactgatt tttgcccttg ttctgtcctt 5580
tttttcaaaa aagaaaatgt gttttttgtt tggtaccata gtgtgaaatg ctgggaacaa 5640
tgactataag acatgctatg gcacatatat ttatagtctg tttatgtaga aacaaatgta 5700
atatattaaa gccttatata taatgaactt tgtactattc acattttgta tcagtattat 5760
gtagcataac aaaggtcata atgctttcag caattgatgt cattttatta aagaacattg 5820
aaaaacttga 5830

<210> 249
<211> 972
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP005202

<309> 2004-10-26

<400> 249

```
Met Gly Pro Gly Val Leu Leu Leu Leu Leu Val Ala Thr Ala Trp His
 1               5                  10                  15
Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
            20                  25                  30
Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
        35                  40                  45
Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
    50                  55                  60
Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65                  70                  75                  80
Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
                85                  90                  95
Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
            100                 105                 110
Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
        115                 120                 125
Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
    130                 135                 140
Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145                 150                 155                 160
Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
                165                 170                 175
Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
            180                 185                 190
Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val
        195                 200                 205
Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
    210                 215                 220
Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225                 230                 235                 240
Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
                245                 250                 255
Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
            260                 265                 270
Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
        275                 280                 285
Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser
    290                 295                 300
Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305                 310                 315                 320
Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
                325                 330                 335
Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
            340                 345                 350
Asn Ala Thr Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu
        355                 360                 365
Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
    370                 375                 380
Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr
385                 390                 395                 400
Pro Pro Glu Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr
                405                 410                 415
Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
```

```
            420                 425                 430
Gln Cys Ser Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
        435                 440                 445
Val Trp Asp Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His
    450                 455                 460
Lys Val Thr Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn
465                 470                 475                 480
Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
                485                 490                 495
Ala Phe Ile Pro Ile Ser Ala Gly Ala His Thr His Pro Pro Asp Glu
            500                 505                 510
Phe Leu Phe Thr Pro Val Val Val Ala Cys Met Ser Ile Met Ala Leu
        515                 520                 525
Leu Leu Leu Leu Leu Leu Leu Leu Leu Tyr Lys Tyr Lys Gln Lys Pro
    530                 535                 540
Lys Tyr Gln Val Arg Trp Lys Ile Ile Glu Ser Tyr Glu Gly Asn Ser
545                 550                 555                 560
Tyr Thr Phe Ile Asp Pro Thr Gln Leu Pro Tyr Asn Glu Lys Trp Glu
                565                 570                 575
Phe Pro Arg Asn Asn Leu Gln Phe Gly Lys Thr Leu Gly Ala Gly Ala
            580                 585                 590
Phe Gly Lys Val Val Glu Ala Thr Ala Phe Gly Leu Gly Lys Glu Asp
        595                 600                 605
Ala Val Leu Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala His Ala
    610                 615                 620
Asp Glu Lys Glu Ala Leu Met Ser Glu Leu Lys Ile Met Ser His Leu
625                 630                 635                 640
Gly Gln His Glu Asn Ile Val Asn Leu Leu Gly Ala Cys Thr His Gly
                645                 650                 655
Gly Pro Val Leu Val Ile Thr Glu Tyr Cys Cys Tyr Gly Asp Leu Leu
            660                 665                 670
Asn Phe Leu Arg Arg Lys Ala Glu Ala Met Leu Gly Pro Ser Leu Ser
        675                 680                 685
Pro Gly Gln Asp Pro Glu Gly Gly Val Asp Tyr Lys Asn Ile His Leu
    690                 695                 700
Glu Lys Lys Tyr Val Arg Arg Asp Ser Gly Phe Ser Ser Gln Gly Val
705                 710                 715                 720
Asp Thr Tyr Val Glu Met Arg Pro Val Ser Thr Ser Ser Asn Asp Ser
                725                 730                 735
Phe Ser Glu Gln Asp Leu Asp Lys Glu Asp Gly Arg Pro Leu Glu Leu
            740                 745                 750
Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
        755                 760                 765
Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
    770                 775                 780
Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
785                 790                 795                 800
Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
                805                 810                 815
Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
            820                 825                 830
Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
        835                 840                 845
Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
    850                 855                 860
Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
```

865 870 875 880
Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
885 890 895
Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
900 905 910
Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
915 920 925
Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu
930 935 940
Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
945 950 955 960
Gln Pro Leu Leu Gln Pro Asn Asn Tyr Gln Phe Cys
965 970

<210> 250
<211> 913
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP054699
<309> 2004-10-26

<400> 250
Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
1 5 10 15
Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
20 25 30
Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
35 40 45
Ala Ser Ser Ser Trp Ser Asp Ser Thr Ala Ala Arg His Ser Arg Leu
50 55 60
Glu Ser Ser Asp Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65 70 75 80
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
85 90 95
Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys
100 105 110
Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
115 120 125
Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
130 135 140
Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145 150 155 160
Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Val Met Ser Val
165 170 175
Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu
180 185 190
Ser Tyr Thr Ala Pro Val Gly Gln Thr Met Tyr Leu Ser Glu Ala Val
195 200 205
Tyr Leu Asn Asp Ser Thr Tyr Asp Gly His Thr Val Gly Gly Leu Gln
210 215 220
Tyr Gly Gly Leu Gly Gln Leu Ala Asp Gly Val Val Gly Leu Asp Asp
225 230 235 240
Phe Arg Lys Ser Gln Glu Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val

```
                245                 250                 255
Gly Trp Ser Asn His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe
            260                 265                 270
Glu Phe Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Val His Cys Asn
        275                 280                 285
Asn Met His Thr Leu Gly Ala Arg Leu Pro Gly Gly Val Glu Cys Arg
    290                 295                 300
Phe Arg Arg Gly Pro Ala Met Ala Trp Glu Gly Glu Pro Met Arg His
305                 310                 315                 320
Asn Leu Gly Gly Asn Leu Gly Asp Pro Arg Ala Arg Ala Val Ser Val
                325                 330                 335
Pro Leu Gly Gly Arg Val Ala Arg Phe Leu Gln Cys Arg Phe Leu Phe
            340                 345                 350
Ala Gly Pro Trp Leu Leu Phe Ser Glu Ile Ser Phe Ile Ser Asp Val
        355                 360                 365
Val Asn Asn Ser Ser Pro Ala Leu Gly Gly Thr Phe Pro Pro Ala Pro
    370                 375                 380
Trp Trp Pro Pro Gly Pro Pro Pro Thr Asn Phe Ser Ser Leu Glu Leu
385                 390                 395                 400
Glu Pro Arg Gly Gln Gln Pro Val Ala Lys Ala Glu Gly Ser Pro Thr
                405                 410                 415
Ala Ile Leu Ile Gly Cys Leu Val Ala Ile Ile Leu Leu Leu Leu Leu
            420                 425                 430
Ile Ile Ala Leu Met Leu Trp Arg Leu His Trp Arg Arg Leu Leu Ser
        435                 440                 445
Lys Ala Glu Arg Arg Val Leu Glu Glu Glu Leu Thr Val His Leu Ser
    450                 455                 460
Val Pro Gly Asp Thr Ile Leu Ile Asn Asn Arg Pro Gly Pro Arg Glu
465                 470                 475                 480
Pro Pro Pro Tyr Gln Glu Pro Arg Pro Arg Gly Asn Pro Pro His Ser
                485                 490                 495
Ala Pro Cys Val Pro Asn Gly Ser Ala Leu Leu Leu Ser Asn Pro Ala
            500                 505                 510
Tyr Arg Leu Leu Leu Ala Thr Tyr Ala Arg Pro Pro Arg Gly Pro Gly
        515                 520                 525
Pro Pro Thr Pro Ala Trp Ala Lys Pro Thr Asn Thr Gln Ala Tyr Ser
    530                 535                 540
Gly Asp Tyr Met Glu Pro Glu Lys Pro Gly Ala Pro Leu Leu Pro Pro
545                 550                 555                 560
Pro Pro Gln Asn Ser Val Pro His Tyr Ala Glu Ala Asp Ile Val Thr
                565                 570                 575
Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ala Val Pro Ala Leu Pro
            580                 585                 590
Pro Gly Ala Val Gly Asp Gly Pro Pro Arg Val Asp Phe Pro Arg Ser
        595                 600                 605
Arg Leu Arg Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu Val
    610                 615                 620
His Leu Cys Glu Val Asp Ser Pro Gln Asp Leu Val Ser Leu Asp Phe
625                 630                 635                 640
Pro Leu Asn Val Arg Lys Gly His Pro Leu Leu Val Ala Val Lys Ile
                645                 650                 655
Leu Arg Pro Asp Ala Thr Lys Asn Ala Arg Asn Asp Phe Leu Lys Glu
            660                 665                 670
Val Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile Arg Leu Leu
        675                 680                 685
Gly Val Cys Val Gln Asp Asp Pro Leu Cys Met Ile Thr Asp Tyr Met
```

```
    690                 695                 700
Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Ala His Gln Leu Glu Asp
705                 710                 715                 720
Lys Ala Ala Glu Gly Ala Pro Gly Asp Gly Gln Ala Ala Gln Gly Pro
                725                 730                 735
Thr Ile Ser Tyr Pro Met Leu Leu His Val Ala Ala Gln Ile Ala Ser
            740                 745                 750
Gly Met Arg Tyr Leu Ala Thr Leu Asn Phe Val His Arg Asp Leu Ala
        755                 760                 765
Thr Arg Asn Cys Leu Val Gly Glu Asn Phe Thr Ile Lys Ile Ala Asp
    770                 775                 780
Phe Gly Met Ser Arg Asn Leu Tyr Ala Gly Asp Tyr Tyr Arg Val Gln
785                 790                 795                 800
Gly Arg Ala Val Leu Pro Ile Arg Trp Met Ala Trp Glu Cys Ile Leu
                805                 810                 815
Met Gly Lys Phe Thr Thr Ala Ser Asp Val Trp Ala Phe Gly Val Thr
            820                 825                 830
Leu Trp Glu Val Leu Met Leu Cys Arg Ala Gln Pro Phe Gly Ser Ala
        835                 840                 845
His Arg Arg Ala Gly His Arg Glu Arg Gly Gly Val Leu Pro Gly Pro
    850                 855                 860
Gly Pro Ala Val Tyr Leu Ser Arg Pro Pro Ala Cys Pro Gln Gly Leu
865                 870                 875                 880
Tyr Glu Leu Met Leu Arg Cys Trp Ser Arg Glu Ser Glu Gln Arg Pro
                885                 890                 895
Pro Phe Ser Gln Leu His Arg Phe Leu Ala Glu Asp Ala Leu Asn Thr
            900                 905                 910
Val
```

<210> 251
<211> 855
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP006173
<309> 2004-10-26

```
<400> 251
Met Ile Leu Ile Pro Arg Met Leu Leu Val Leu Phe Leu Leu Leu Pro
 1               5                  10                  15
Ile Leu Ser Ser Ala Lys Ala Gln Val Asn Pro Ala Ile Cys Arg Tyr
            20                  25                  30
Pro Leu Gly Met Ser Gly Gly Gln Ile Pro Asp Glu Asp Ile Thr Ala
        35                  40                  45
Ser Ser Gln Trp Ser Glu Ser Thr Ala Ala Lys Tyr Gly Arg Leu Asp
    50                  55                  60
Ser Glu Glu Gly Asp Gly Ala Trp Cys Pro Glu Ile Pro Val Glu Pro
65                  70                  75                  80
Asp Asp Leu Lys Glu Phe Leu Gln Ile Asp Leu His Thr Leu His Phe
                85                  90                  95
Ile Thr Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly His Gly Ile
            100                 105                 110
Glu Phe Ala Pro Met Tyr Lys Ile Asn Tyr Ser Arg Asp Gly Thr Arg
```

```
        115                 120                 125
Trp Ile Ser Trp Arg Asn Arg His Gly Lys Gln Val Leu Asp Gly Asn
    130                 135                 140
Ser Asn Pro Tyr Asp Ile Phe Leu Lys Asp Leu Glu Pro Pro Ile Val
145                 150                 155                 160
Ala Arg Phe Val Arg Phe Ile Pro Val Thr Asp His Ser Met Asn Val
                165                 170                 175
Cys Met Arg Val Glu Leu Tyr Gly Cys Val Trp Leu Asp Gly Leu Val
            180                 185                 190
Ser Tyr Asn Ala Pro Ala Gly Gln Gln Phe Val Leu Pro Gly Gly Ser
        195                 200                 205
Ile Ile Tyr Leu Asn Asp Ser Val Tyr Asp Gly Ala Val Gly Tyr Ser
    210                 215                 220
Met Thr Glu Gly Leu Gly Gln Leu Thr Asp Gly Val Ser Gly Leu Asp
225                 230                 235                 240
Asp Phe Thr Gln Thr His Glu Tyr His Val Trp Pro Gly Tyr Asp Tyr
                245                 250                 255
Val Gly Trp Arg Asn Glu Ser Ala Thr Asn Gly Tyr Ile Glu Ile Met
            260                 265                 270
Phe Glu Phe Asp Arg Ile Arg Asn Phe Thr Thr Met Lys Val His Cys
        275                 280                 285
Asn Asn Met Phe Ala Lys Gly Val Lys Ile Phe Lys Glu Val Gln Cys
    290                 295                 300
Tyr Phe Arg Ser Glu Ala Ser Glu Trp Glu Pro Asn Ala Ile Ser Phe
305                 310                 315                 320
Pro Leu Val Leu Asp Asp Val Asn Pro Ser Ala Arg Phe Val Thr Val
                325                 330                 335
Pro Leu His His Arg Met Ala Ser Ala Ile Lys Cys Gln Tyr His Phe
            340                 345                 350
Ala Asp Thr Trp Met Met Phe Ser Glu Ile Thr Phe Gln Ser Asp Ala
        355                 360                 365
Ala Met Tyr Asn Asn Ser Glu Ala Leu Pro Thr Ser Pro Met Ala Pro
    370                 375                 380
Thr Thr Tyr Asp Pro Met Leu Lys Val Asp Asp Ser Asn Thr Arg Ile
385                 390                 395                 400
Leu Ile Gly Cys Leu Val Ala Ile Ile Phe Ile Leu Leu Ala Ile Ile
                405                 410                 415
Val Ile Ile Leu Trp Arg Gln Phe Trp Gln Lys Met Leu Glu Lys Ala
            420                 425                 430
Ser Arg Arg Met Leu Asp Asp Glu Met Thr Val Ser Leu Ser Leu Pro
        435                 440                 445
Ser Asp Ser Ser Met Phe Asn Asn Asn Arg Ser Ser Ser Pro Ser Glu
    450                 455                 460
Gln Gly Ser Asn Ser Thr Tyr Asp Arg Ile Phe Pro Leu Arg Pro Asp
465                 470                 475                 480
Tyr Gln Glu Pro Ser Arg Leu Ile Arg Lys Leu Pro Glu Phe Ala Pro
                485                 490                 495
Gly Glu Glu Glu Ser Gly Cys Ser Gly Val Val Lys Pro Val Gln Pro
            500                 505                 510
Ser Gly Pro Glu Gly Val Pro His Tyr Ala Glu Ala Asp Ile Val Asn
        515                 520                 525
Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ser Val Pro Ala Val Thr
    530                 535                 540
Met Asp Leu Leu Ser Gly Lys Asp Val Ala Val Glu Glu Phe Pro Arg
545                 550                 555                 560
Lys Leu Leu Thr Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu
```

```
                565                 570                 575
Val His Leu Cys Glu Val Glu Gly Met Glu Lys Phe Lys Asp Lys Asp
            580                 585                 590
Phe Ala Leu Asp Val Ser Ala Asn Gln Pro Val Leu Val Ala Val Lys
        595                 600                 605
Met Leu Arg Ala Asp Ala Asn Lys Asn Ala Arg Asn Asp Phe Leu Lys
    610                 615                 620
Glu Ile Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile His Leu
625                 630                 635                 640
Leu Ser Val Cys Ile Thr Asp Asp Pro Leu Cys Met Ile Thr Glu Tyr
                645                 650                 655
Met Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Arg His Glu Pro Pro
            660                 665                 670
Asn Ser Ser Ser Ser Asp Val Arg Thr Val Ser Tyr Thr Asn Leu Lys
        675                 680                 685
Phe Met Ala Thr Gln Ile Ala Ser Gly Met Lys Tyr Leu Ser Ser Leu
    690                 695                 700
Asn Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Lys
705                 710                 715                 720
Asn Tyr Thr Ile Lys Ile Ala Asp Phe Gly Met Ser Arg Asn Leu Tyr
                725                 730                 735
Ser Gly Asp Tyr Tyr Arg Ile Gln Gly Arg Ala Val Leu Pro Ile Arg
            740                 745                 750
Trp Met Ser Trp Glu Ser Ile Leu Leu Gly Lys Phe Thr Thr Ala Ser
        755                 760                 765
Asp Val Trp Ala Phe Gly Val Thr Leu Trp Glu Thr Phe Thr Phe Cys
    770                 775                 780
Gln Glu Gln Pro Tyr Ser Gln Leu Ser Asp Glu Gln Val Ile Glu Asn
785                 790                 795                 800
Thr Gly Glu Phe Phe Arg Asp Gln Gly Arg Gln Thr Tyr Leu Pro Gln
                805                 810                 815
Pro Ala Ile Cys Pro Asp Ser Val Tyr Lys Leu Met Leu Ser Cys Trp
            820                 825                 830
Arg Arg Asp Thr Lys Asn Arg Pro Ser Phe Gln Glu Ile His Leu Leu
        835                 840                 845
Leu Leu Gln Gln Gly Asp Glu
    850                 855


<210> 252
<211> 1210
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP005219
<309> 2004-01-26

<400> 252
Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
 1               5                  10                  15
Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
            20                  25                  30
Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
        35                  40                  45
Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
```

```
    50                  55                  60
Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
65                  70                  75                  80
Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
                85                  90                  95
Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
            100                 105                 110
Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
        115                 120                 125
Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
    130                 135                 140
His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145                 150                 155                 160
Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
                165                 170                 175
Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
            180                 185                 190
Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
        195                 200                 205
Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
    210                 215                 220
Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225                 230                 235                 240
Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255
Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270
Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285
Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300
Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320
Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335
Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350
Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365
Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380
Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400
Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415
Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430
His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445
Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
    450                 455                 460
Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480
Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495
Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
```

```
            500                 505                 510
Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
        515                 520                 525
Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540
Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560
Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575
Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590
Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605
Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620
Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
625                 630                 635                 640
Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
                645                 650                 655
Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His
            660                 665                 670
Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
        675                 680                 685
Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
    690                 695                 700
Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
705                 710                 715                 720
Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
                725                 730                 735
Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
            740                 745                 750
Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
        755                 760                 765
Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
    770                 775                 780
Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
785                 790                 795                 800
Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
                805                 810                 815
Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
            820                 825                 830
Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
        835                 840                 845
Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
    850                 855                 860
Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
865                 870                 875                 880
Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
                885                 890                 895
Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
            900                 905                 910
Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
        915                 920                 925
Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
    930                 935                 940
Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
```

945 950 955 960
Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
965 970 975
Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
980 985 990
Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp
995 1000 1005
Asp Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe
1010 1015 1020
Ser Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala
1025 1030 1035 1040
Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln
1045 1050 1055
Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp
1060 1065 1070
Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro
1075 1080 1085
Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
1090 1095 1100
Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser
1105 1110 1115 1120
Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
1125 1130 1135
Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp
1140 1145 1150
Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp
1155 1160 1165
Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn
1170 1175 1180
Gly Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val
1185 1190 1195 1200
Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
1205 1210

<210> 253
<211> 976
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP005223
<309> 2004-11-29

<400> 253
Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
1 5 10 15
Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
20 25 30
Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
35 40 45
Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
50 55 60
Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65 70 75 80
Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His

```
                85                  90                  95
Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
            100                 105                 110
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
        115                 120                 125
Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
    130                 135                 140
Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Ala
145                 150                 155                 160
Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
                165                 170                 175
Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
            180                 185                 190
Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
        195                 200                 205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
    210                 215                 220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225                 230                 235                 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
                245                 250                 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
            260                 265                 270
Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
        275                 280                 285
Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
    290                 295                 300
Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305                 310                 315                 320
Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
                325                 330                 335
Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
            340                 345                 350
Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
        355                 360                 365
Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
    370                 375                 380
Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Gly Leu Thr
385                 390                 395                 400
Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
                405                 410                 415
Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
            420                 425                 430
His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Glu Ser Leu
        435                 440                 445
Ser Gly Leu Ser Leu Arg Leu Val Lys Lys Glu Pro Arg Gln Leu Glu
    450                 455                 460
Leu Thr Trp Ala Gly Ser Arg Pro Arg Ser Pro Gly Ala Asn Leu Thr
465                 470                 475                 480
Tyr Glu Leu His Val Leu Asn Gln Asp Glu Glu Arg Tyr Gln Met Val
                485                 490                 495
Leu Glu Pro Arg Val Leu Leu Thr Glu Leu Gln Pro Asp Thr Thr Tyr
            500                 505                 510
Ile Val Arg Val Arg Met Leu Thr Pro Leu Gly Pro Gly Pro Phe Ser
        515                 520                 525
Pro Asp His Glu Phe Arg Thr Ser Pro Pro Val Ser Arg Gly Leu Thr
```

```
    530                 535                 540
Gly Gly Glu Ile Val Ala Val Ile Phe Gly Leu Leu Leu Gly Ala Ala
545                 550                 555                 560
Leu Leu Leu Gly Ile Leu Val Phe Arg Ser Arg Arg Ala Gln Arg Gln
                565                 570                 575
Arg Gln Gln Arg Gln Arg Asp Arg Ala Thr Asp Val Asp Arg Glu Asp
            580                 585                 590
Lys Leu Trp Leu Lys Pro Tyr Val Asp Leu Gln Ala Tyr Glu Asp Pro
        595                 600                 605
Ala Gln Gly Ala Leu Asp Phe Thr Arg Glu Leu Asp Pro Ala Trp Leu
    610                 615                 620
Met Val Asp Thr Val Ile Gly Glu Gly Glu Phe Gly Glu Val Tyr Arg
625                 630                 635                 640
Gly Thr Leu Arg Leu Pro Ser Gln Asp Cys Lys Thr Val Ala Ile Lys
                645                 650                 655
Thr Leu Lys Asp Thr Ser Pro Gly Gly Gln Trp Trp Asn Phe Leu Arg
            660                 665                 670
Glu Ala Thr Ile Met Gly Gln Phe Ser His Pro His Ile Leu His Leu
        675                 680                 685
Glu Gly Val Val Thr Lys Arg Lys Pro Ile Met Ile Ile Thr Glu Phe
    690                 695                 700
Met Glu Asn Gly Ala Leu Asp Ala Phe Leu Arg Glu Arg Glu Asp Gln
705                 710                 715                 720
Leu Val Pro Gly Gln Leu Val Ala Met Leu Gln Gly Ile Ala Ser Gly
                725                 730                 735
Met Asn Tyr Leu Ser Asn His Asn Tyr Val His Arg Asp Leu Ala Ala
            740                 745                 750
Arg Asn Ile Leu Val Asn Gln Asn Leu Cys Cys Lys Val Ser Asp Phe
        755                 760                 765
Gly Leu Thr Arg Leu Leu Asp Asp Phe Asp Gly Thr Tyr Glu Thr Gln
    770                 775                 780
Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala His
785                 790                 795                 800
Arg Ile Phe Thr Thr Ala Ser Asp Val Trp Ser Phe Gly Ile Val Met
                805                 810                 815
Trp Glu Val Leu Ser Phe Gly Asp Lys Pro Tyr Gly Glu Met Ser Asn
            820                 825                 830
Gln Glu Val Met Lys Ser Ile Glu Asp Gly Tyr Arg Leu Pro Pro Pro
        835                 840                 845
Val Asp Cys Pro Ala Pro Leu Tyr Glu Leu Met Lys Asn Cys Trp Ala
    850                 855                 860
Tyr Asp Arg Ala Arg Arg Pro His Phe Gln Lys Leu Gln Ala His Leu
865                 870                 875                 880
Glu Gln Leu Leu Ala Asn Pro His Ser Leu Arg Thr Ile Ala Asn Phe
                885                 890                 895
Asp Pro Arg Met Thr Leu Arg Leu Pro Ser Leu Ser Gly Ser Asp Gly
            900                 905                 910
Ile Pro Tyr Arg Thr Val Ser Glu Trp Leu Glu Ser Ile Arg Met Lys
        915                 920                 925
Arg Tyr Ile Leu His Phe His Ser Ala Gly Leu Asp Thr Met Glu Cys
    930                 935                 940
Val Leu Glu Leu Thr Ala Glu Asp Leu Thr Gln Met Gly Ile Thr Leu
945                 950                 955                 960
Pro Gly His Gln Lys Arg Ile Leu Cys Ser Ile Gln Gly Phe Lys Asp
                965                 970                 975
```

<210> 254
<211> 976
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004422
<309> 2004-12-20

<400> 254
Met Glu Leu Gln Ala Ala Arg Ala Cys Phe Ala Leu Leu Trp Gly Cys
1 5 10 15
Ala Leu Ala Ala Ala Ala Ala Ala Gln Gly Lys Glu Val Val Leu Leu
20 25 30
Asp Phe Ala Ala Ala Gly Gly Glu Leu Gly Trp Leu Thr His Pro Tyr
35 40 45
Gly Lys Gly Trp Asp Leu Met Gln Asn Ile Met Asn Asp Met Pro Ile
50 55 60
Tyr Met Tyr Ser Val Cys Asn Val Met Ser Gly Asp Gln Asp Asn Trp
65 70 75 80
Leu Arg Thr Asn Trp Val Tyr Arg Gly Glu Ala Glu Arg Ile Phe Ile
85 90 95
Glu Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Phe Pro Gly Gly Ala
100 105 110
Ser Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Ala Glu Ser Asp Leu
115 120 125
Asp Tyr Gly Thr Asn Phe Gln Lys Arg Leu Phe Thr Lys Ile Asp Thr
130 135 140
Ile Ala Pro Asp Glu Ile Thr Val Ser Ser Asp Phe Glu Ala Arg His
145 150 155 160
Val Lys Leu Asn Val Glu Glu Arg Ser Val Gly Pro Leu Thr Arg Lys
165 170 175
Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Val Ala Leu Leu
180 185 190
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Glu Leu Leu Gln Gly Leu
195 200 205
Ala His Phe Pro Glu Thr Ile Ala Gly Ser Asp Ala Pro Ser Leu Ala
210 215 220
Thr Val Ala Gly Thr Cys Val Asp His Ala Val Val Pro Pro Gly Gly
225 230 235 240
Glu Glu Pro Arg Met His Cys Ala Val Asp Gly Glu Trp Leu Val Pro
245 250 255
Ile Gly Gln Cys Leu Cys Gln Ala Gly Tyr Glu Lys Val Glu Asp Ala
260 265 270
Cys Gln Ala Cys Ser Pro Gly Phe Phe Lys Phe Glu Ala Ser Glu Ser
275 280 285
Pro Cys Leu Glu Cys Pro Glu His Thr Leu Pro Ser Pro Glu Gly Ala
290 295 300
Thr Ser Cys Glu Cys Glu Glu Gly Phe Phe Arg Ala Pro Gln Asp Pro
305 310 315 320
Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro His Tyr Leu Thr
325 330 335
Ala Val Gly Met Gly Ala Lys Val Glu Leu Arg Trp Thr Pro Pro Gln
340 345 350
Asp Ser Gly Gly Arg Glu Asp Ile Val Tyr Ser Val Thr Cys Glu Gln

```
        355                 360                 365
Cys Trp Pro Glu Ser Gly Glu Cys Gly Pro Cys Glu Ala Ser Val Arg
    370                 375                 380
Tyr Ser Glu Pro Pro His Gly Leu Thr Arg Thr Ser Val Thr Val Ser
385                 390                 395                 400
Asp Leu Glu Pro His Met Asn Tyr Thr Phe Thr Val Glu Ala Arg Asn
                405                 410                 415
Gly Val Ser Gly Leu Val Thr Ser Arg Ser Phe Arg Thr Ala Ser Val
            420                 425                 430
Ser Ile Asn Gln Thr Glu Pro Pro Lys Val Arg Leu Glu Gly Arg Ser
        435                 440                 445
Thr Thr Ser Leu Ser Val Ser Trp Ser Ile Pro Pro Pro Gln Gln Ser
    450                 455                 460
Arg Val Trp Lys Tyr Glu Val Thr Tyr Arg Lys Lys Gly Asp Ser Asn
465                 470                 475                 480
Ser Tyr Asn Val Arg Arg Thr Glu Gly Phe Ser Val Thr Leu Asp Asp
                485                 490                 495
Leu Ala Pro Asp Thr Thr Tyr Leu Val Gln Val Gln Ala Leu Thr Gln
            500                 505                 510
Glu Gly Gln Gly Ala Gly Ser Lys Val His Glu Phe Gln Thr Leu Ser
        515                 520                 525
Pro Glu Gly Ser Gly Asn Leu Ala Val Ile Gly Gly Val Ala Val Gly
    530                 535                 540
Val Val Leu Leu Leu Val Leu Ala Gly Val Gly Phe Phe Ile His Arg
545                 550                 555                 560
Arg Arg Lys Asn Gln Arg Ala Arg Gln Ser Pro Glu Asp Val Tyr Phe
                565                 570                 575
Ser Lys Ser Glu Gln Leu Lys Pro Leu Lys Thr Tyr Val Asp Pro His
            580                 585                 590
Thr Tyr Glu Asp Pro Asn Gln Ala Val Leu Lys Phe Thr Thr Glu Ile
        595                 600                 605
His Pro Ser Cys Val Thr Arg Gln Lys Val Ile Gly Ala Gly Glu Phe
    610                 615                 620
Gly Glu Val Tyr Lys Gly Met Leu Lys Thr Ser Ser Gly Lys Lys Glu
625                 630                 635                 640
Val Pro Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Glu Lys Gln
                645                 650                 655
Arg Val Asp Phe Leu Gly Glu Ala Gly Ile Met Gly Gln Phe Ser His
            660                 665                 670
His Asn Ile Ile Arg Leu Glu Gly Val Ile Ser Lys Tyr Lys Pro Met
        675                 680                 685
Met Ile Ile Thr Glu Tyr Met Glu Asn Gly Ala Leu Asp Lys Phe Leu
    690                 695                 700
Arg Glu Lys Asp Gly Glu Phe Ser Val Leu Gln Leu Val Gly Met Leu
705                 710                 715                 720
Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asn Met Asn Tyr Val
                725                 730                 735
His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val
            740                 745                 750
Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro
        755                 760                 765
Glu Ala Thr Tyr Thr Thr Ser Gly Gly Lys Ile Pro Ile Arg Trp Thr
    770                 775                 780
Ala Pro Glu Ala Ile Ser Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val
785                 790                 795                 800
Trp Ser Phe Gly Ile Val Met Trp Glu Val Met Thr Tyr Gly Glu Arg
```

```
                805                 810                 815
Pro Tyr Trp Glu Leu Ser Asn His Glu Val Met Lys Ala Ile Asn Asp
            820                 825                 830
Gly Phe Arg Leu Pro Thr Pro Met Asp Cys Pro Ser Ala Ile Tyr Gln
        835                 840                 845
Leu Met Met Gln Cys Trp Gln Gln Glu Arg Ala Arg Arg Pro Lys Phe
    850                 855                 860
Ala Asp Ile Val Ser Ile Leu Asp Lys Leu Ile Arg Ala Pro Asp Ser
865                 870                 875                 880
Leu Lys Thr Leu Ala Asp Phe Asp Pro Arg Val Ser Ile Arg Leu Pro
                885                 890                 895
Ser Thr Ser Gly Ser Glu Gly Val Pro Phe Arg Thr Val Ser Glu Trp
            900                 905                 910
Leu Glu Ser Ile Lys Met Gln Gln Tyr Thr Glu His Phe Met Ala Ala
        915                 920                 925
Gly Tyr Thr Ala Ile Glu Lys Val Val Gln Met Thr Asn Asp Asp Ile
    930                 935                 940
Lys Arg Ile Gly Val Arg Leu Pro Gly His Gln Lys Arg Ile Ala Tyr
945                 950                 955                 960
Ser Leu Leu Gly Leu Lys Asp Gln Val Asn Thr Val Gly Ile Pro Ile
                965                 970                 975
```

<210> 255
<211> 983
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP005224
<309> 2004-11-16

<400> 255

```
Met Asp Cys Gln Leu Ser Ile Leu Leu Leu Leu Ser Cys Ser Val Leu
 1               5                  10                  15
Asp Ser Phe Gly Glu Leu Ile Pro Gln Pro Ser Asn Glu Val Asn Leu
            20                  25                  30
Leu Asp Ser Lys Thr Ile Gln Gly Glu Leu Gly Trp Ile Ser Tyr Pro
        35                  40                  45
Ser His Gly Trp Glu Glu Ile Ser Gly Val Asp Glu His Tyr Thr Pro
    50                  55                  60
Ile Arg Thr Tyr Gln Val Cys Asn Val Met Asp His Ser Gln Asn Asn
65                  70                  75                  80
Trp Leu Arg Thr Asn Trp Val Pro Arg Asn Ser Ala Gln Lys Ile Tyr
                85                  90                  95
Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Ile Pro Leu Val
            100                 105                 110
Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp
        115                 120                 125
Asp Asp His Gly Val Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp
    130                 135                 140
Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg
145                 150                 155                 160
Ile Leu Lys Leu Asn Thr Glu Ile Arg Glu Val Gly Pro Val Asn Lys
                165                 170                 175
Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu
```

```
            180                 185                 190
Val Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn
        195                 200                 205
Leu Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val
    210                 215                 220
Glu Val Arg Gly Ser Cys Val Asn Asn Ser Lys Glu Glu Asp Pro Pro
225                 230                 235                 240
Arg Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
                245                 250                 255
Cys Ser Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Met Cys Gln Ala
            260                 265                 270
Cys Arg Pro Gly Phe Tyr Lys Ala Leu Asp Gly Asn Met Lys Cys Ala
        275                 280                 285
Lys Cys Pro Pro His Ser Ser Thr Gln Glu Asp Gly Ser Met Asn Cys
    290                 295                 300
Arg Cys Glu Asn Asn Tyr Phe Arg Ala Asp Lys Asp Pro Pro Ser Met
305                 310                 315                 320
Ala Cys Thr Arg Pro Pro Ser Ser Pro Arg Asn Val Ile Ser Asn Ile
                325                 330                 335
Asn Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly
            340                 345                 350
Gly Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Trp
        355                 360                 365
Asn Ile Lys Gln Cys Glu Pro Cys Ser Pro Asn Val Arg Phe Leu Pro
    370                 375                 380
Arg Gln Phe Gly Leu Thr Asn Thr Thr Val Thr Val Thr Asp Leu Leu
385                 390                 395                 400
Ala His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser
                405                 410                 415
Glu Leu Ser Ser Pro Pro Arg Gln Phe Ala Ala Val Ser Ile Thr Thr
            420                 425                 430
Asn Gln Ala Ala Pro Ser Pro Val Leu Thr Ile Lys Lys Asp Arg Thr
        435                 440                 445
Ser Arg Asn Ser Ile Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn
    450                 455                 460
Gly Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln
465                 470                 475                 480
Glu Thr Ser Tyr Thr Ile Leu Arg Ala Arg Gly Thr Asn Val Thr Ile
                485                 490                 495
Ser Ser Leu Lys Pro Asp Thr Ile Tyr Val Phe Gln Ile Arg Ala Arg
            500                 505                 510
Thr Ala Ala Gly Tyr Gly Thr Asn Ser Arg Lys Phe Glu Phe Glu Thr
        515                 520                 525
Ser Pro Asp Ser Phe Ser Ile Ser Gly Glu Ser Ser Gln Val Val Met
    530                 535                 540
Ile Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Ile
545                 550                 555                 560
Tyr Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Ser Lys His Gly Ala
                565                 570                 575
Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly
            580                 585                 590
Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Thr Gln Ala
        595                 600                 605
Val His Glu Phe Ala Lys Glu Leu Asp Ala Thr Asn Ile Ser Ile Asp
    610                 615                 620
Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
```

625 630 635 640
Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys
645 650 655
Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser
660 665 670
Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val
675 680 685
Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn
690 695 700
Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val
705 710 715 720
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr
725 730 735
Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
740 745 750
Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
755 760 765
Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
770 775 780
Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys
785 790 795 800
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Leu Trp Glu
805 810 815
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Ser Asn Gln Asp
820 825 830
Val Ile Lys Ala Val Asp Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
835 840 845
Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
850 855 860
Arg Asn Asn Arg Pro Lys Phe Glu Gln Ile Val Ser Ile Leu Asp Lys
865 870 875 880
Leu Ile Arg Asn Pro Gly Ser Leu Lys Ile Ile Thr Ser Ala Ala Ala
885 890 895
Arg Pro Ser Asn Leu Leu Leu Asp Gln Ser Asn Val Asp Ile Thr Thr
900 905 910
Phe Arg Thr Thr Gly Asp Trp Leu Asn Gly Val Trp Thr Ala His Cys
915 920 925
Lys Glu Ile Phe Thr Gly Val Glu Tyr Ser Ser Cys Asp Thr Ile Ala
930 935 940
Lys Ile Ser Thr Asp Asp Met Lys Lys Val Gly Val Thr Val Val Gly
945 950 955 960
Pro Gln Lys Lys Ile Ile Ser Ser Ile Lys Ala Leu Glu Thr Gln Ser
965 970 975
Lys Asn Gly Pro Val Pro Val
980

<210> 256
<211> 986
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004429
<309> 2004-11-16

<400> 256

```
Met Ala Gly Ile Phe Tyr Phe Ala Leu Phe Ser Cys Leu Phe Gly Ile
 1               5                  10                  15
Cys Asp Ala Val Thr Gly Ser Arg Val Tyr Pro Ala Asn Glu Val Thr
            20                  25                  30
Leu Leu Asp Ser Arg Ser Val Gln Gly Glu Leu Gly Trp Ile Ala Ser
        35                  40                  45
Pro Leu Glu Gly Gly Trp Glu Glu Val Ser Ile Met Asp Glu Lys Asn
    50                  55                  60
Thr Pro Ile Arg Thr Tyr Gln Val Cys Asn Val Met Glu Pro Ser Gln
65                  70                  75                  80
Asn Asn Trp Leu Arg Thr Asp Trp Ile Thr Arg Glu Gly Ala Gln Arg
                85                  90                  95
Val Tyr Ile Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro
            100                 105                 110
Gly Val Met Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu
        115                 120                 125
Ser Asp Asn Asp Lys Glu Arg Phe Ile Arg Glu Asn Gln Phe Val Lys
    130                 135                 140
Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Val Asp Ile Gly
145                 150                 155                 160
Asp Arg Ile Met Lys Leu Asn Thr Glu Ile Arg Asp Val Gly Pro Leu
                165                 170                 175
Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile
            180                 185                 190
Ala Leu Val Ser Val Arg Val Phe Tyr Lys Lys Cys Pro Leu Thr Val
        195                 200                 205
Arg Asn Leu Ala Gln Phe Pro Asp Thr Ile Thr Gly Ala Asp Thr Ser
    210                 215                 220
Ser Leu Val Glu Val Arg Gly Ser Cys Val Asn Asn Ser Glu Glu Lys
225                 230                 235                 240
Asp Val Pro Lys Met Tyr Cys Gly Ala Asp Gly Glu Trp Leu Val Pro
                245                 250                 255
Ile Gly Asn Cys Leu Cys Asn Ala Gly His Glu Glu Arg Ser Gly Glu
            260                 265                 270
Cys Gln Ala Cys Lys Ile Gly Tyr Tyr Lys Ala Leu Ser Thr Asp Ala
        275                 280                 285
Thr Cys Ala Lys Cys Pro Pro His Ser Tyr Ser Val Trp Glu Gly Ala
    290                 295                 300
Thr Ser Cys Thr Cys Asp Arg Gly Phe Phe Arg Ala Asp Asn Asp Ala
305                 310                 315                 320
Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro Leu Asn Leu Ile
                325                 330                 335
Ser Asn Val Asn Glu Thr Ser Val Asn Leu Glu Trp Ser Ser Pro Gln
            340                 345                 350
Asn Thr Gly Gly Arg Gln Asp Ile Ser Tyr Asn Val Val Cys Lys Lys
        355                 360                 365
Cys Gly Ala Gly Asp Pro Ser Lys Cys Arg Pro Cys Gly Ser Gly Val
    370                 375                 380
His Tyr Thr Pro Gln Gln Asn Gly Leu Lys Thr Thr Lys Val Ser Ile
385                 390                 395                 400
Thr Asp Leu Leu Ala His Thr Asn Tyr Thr Phe Glu Ile Trp Ala Val
                405                 410                 415
Asn Gly Val Ser Lys Tyr Asn Pro Asn Pro Asp Gln Ser Val Ser Val
            420                 425                 430
Thr Val Thr Thr Asn Gln Ala Ala Pro Ser Ser Ile Ala Leu Val Gln
```

```
        435                 440                 445
Ala Lys Glu Val Thr Arg Tyr Ser Val Ala Leu Ala Trp Leu Glu Pro
    450                 455                 460
Asp Arg Pro Asn Gly Val Ile Leu Glu Tyr Glu Val Lys Tyr Tyr Glu
465                 470                 475                 480
Lys Asp Gln Asn Glu Arg Ser Tyr Arg Ile Val Arg Thr Ala Ala Arg
                485                 490                 495
Asn Thr Asp Ile Lys Gly Leu Asn Pro Leu Thr Ser Tyr Val Phe His
            500                 505                 510
Val Arg Ala Arg Thr Ala Ala Gly Tyr Gly Asp Phe Ser Glu Pro Leu
        515                 520                 525
Glu Val Thr Thr Asn Thr Val Pro Ser Arg Ile Ile Gly Asp Gly Ala
    530                 535                 540
Asn Ser Thr Val Leu Leu Val Ser Val Ser Gly Ser Val Val Leu Val
545                 550                 555                 560
Val Ile Leu Ile Ala Ala Phe Val Ile Ser Arg Arg Arg Ser Lys Tyr
                565                 570                 575
Ser Lys Ala Lys Gln Glu Ala Asp Glu Glu Lys His Leu Asn Gln Gly
            580                 585                 590
Val Arg Thr Tyr Val Asp Pro Phe Thr Tyr Glu Asp Pro Asn Gln Ala
        595                 600                 605
Val Arg Glu Phe Ala Lys Glu Ile Asp Ala Ser Cys Ile Lys Ile Glu
    610                 615                 620
Lys Val Ile Gly Val Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625                 630                 635                 640
Lys Val Pro Gly Lys Arg Glu Ile Cys Val Ala Ile Lys Thr Leu Lys
                645                 650                 655
Ala Gly Tyr Thr Asp Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
            660                 665                 670
Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu Gly Val
        675                 680                 685
Val Thr Lys Cys Lys Pro Val Met Ile Ile Thr Glu Tyr Met Glu Asn
    690                 695                 700
Gly Ser Leu Asp Ala Phe Leu Arg Lys Asn Asp Gly Arg Phe Thr Val
705                 710                 715                 720
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Gly Ser Gly Met Lys Tyr
                725                 730                 735
Leu Ser Asp Met Ser Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750
Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Met Ser
        755                 760                 765
Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
    770                 775                 780
Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu
                805                 810                 815
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830
Val Ile Lys Ala Ile Glu Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845
Cys Pro Ile Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Glu
    850                 855                 860
Arg Ser Asp Arg Pro Lys Phe Gly Gln Ile Val Asn Met Leu Asp Lys
865                 870                 875                 880
Leu Ile Arg Asn Pro Asn Ser Leu Lys Arg Thr Gly Thr Glu Ser Ser
```

```
                885                 890                 895
Arg Pro Asn Thr Ala Leu Leu Asp Pro Ser Ser Pro Glu Phe Ser Ala
            900                 905                 910
Val Val Ser Val Gly Asp Trp Leu Gln Ala Ile Lys Met Asp Arg Tyr
        915                 920                 925
Lys Asp Asn Phe Thr Ala Ala Gly Tyr Thr Thr Leu Glu Ala Val Val
    930                 935                 940
His Val Asn Gln Glu Asp Leu Ala Arg Ile Gly Ile Thr Ala Ile Thr
945                 950                 955                 960
His Gln Asn Lys Ile Leu Ser Ser Val Gln Ala Met Arg Thr Gln Met
                965                 970                 975
Gln Gln Met His Gly Arg Met Val Pro Val
            980                 985


<210> 257
<211> 991
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. AAA74245
<309> 1995-08-10

<400> 257
Pro Ala Ser Leu Ala Gly Cys Tyr Ser Ala Pro Arg Arg Ala Pro Leu
 1               5                  10                  15
Trp Thr Cys Leu Leu Leu Cys Ala Ala Leu Arg Thr Leu Leu Ala Ser
            20                  25                  30
Pro Ser Asn Glu Val Asn Leu Leu Asp Ser Arg Thr Val Met Gly Asp
        35                  40                  45
Leu Gly Trp Ile Ala Phe Pro Lys Asn Gly Trp Glu Glu Ile Gly Glu
    50                  55                  60
Val Asp Glu Asn Tyr Ala Pro Ile His Thr Tyr Gln Val Cys Lys Val
65                  70                  75                  80
Met Glu Gln Asn Gln Asn Asn Trp Leu Leu Thr Ser Trp Ile Ser Asn
                85                  90                  95
Glu Gly Ala Ser Arg Ile Phe Ile Glu Leu Lys Phe Thr Leu Arg Asp
            100                 105                 110
Cys Asn Ser Leu Pro Gly Gly Leu Gly Thr Cys Lys Glu Thr Phe Asn
        115                 120                 125
Met Tyr Tyr Phe Glu Ser Asp Asp Gln Asn Gly Arg Asn Ile Lys Glu
    130                 135                 140
Asn Gln Tyr Ile Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr
145                 150                 155                 160
Glu Leu Asp Leu Gly Asp Arg Val Met Lys Leu Asn Thr Glu Val Arg
                165                 170                 175
Asp Val Gly Pro Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp
            180                 185                 190
Val Gly Ala Cys Ile Ala Leu Val Ser Val Arg Val Tyr Tyr Lys Lys
        195                 200                 205
Cys Pro Ser Val Val Arg His Leu Ala Val Phe Pro Asp Thr Ile Thr
    210                 215                 220
Gly Ala Asp Ser Ser Gln Leu Leu Glu Val Ser Gly Ser Cys Val Asn
225                 230                 235                 240
His Ser Val Thr Asp Glu Pro Pro Lys Met His Cys Ser Ala Glu Gly
```

```
                245                 250                 255
Glu Trp Leu Val Pro Ile Gly Lys Cys Met Cys Lys Ala Gly Tyr Glu
            260                 265                 270
Glu Lys Asn Gly Thr Cys Gln Val Cys Arg Pro Gly Phe Phe Lys Ala
        275                 280                 285
Ser Pro His Ile Gln Ser Cys Gly Lys Cys Pro Pro His Ser Tyr Thr
    290                 295                 300
His Glu Glu Ala Ser Thr Ser Cys Val Cys Glu Lys Asp Tyr Phe Arg
305                 310                 315                 320
Arg Glu Ser Asp Pro Pro Thr Met Ala Cys Thr Arg Pro Pro Ser Ala
                325                 330                 335
Pro Arg Asn Ala Ile Ser Asn Val Asn Glu Thr Ser Val Phe Leu Glu
            340                 345                 350
Trp Ile Pro Pro Ala Asp Thr Gly Gly Arg Lys Asp Val Ser Tyr Tyr
        355                 360                 365
Ile Ala Cys Lys Lys Cys Asn Ser His Ala Gly Val Cys Glu Glu Cys
    370                 375                 380
Gly Gly His Val Arg Tyr Leu Pro Arg Gln Ser Gly Leu Lys Asn Thr
385                 390                 395                 400
Ser Val Met Met Val Asp Leu Leu Ala His Thr Asn Tyr Thr Phe Glu
                405                 410                 415
Ile Glu Ala Val Asn Gly Val Ser Asp Leu Ser Pro Gly Ala Arg Gln
            420                 425                 430
Tyr Val Ser Val Asn Val Thr Thr Asn Gln Ala Ala Pro Ser Pro Val
        435                 440                 445
Thr Asn Val Lys Lys Gly Lys Ile Ala Lys Asn Ser Ile Ser Leu Ser
    450                 455                 460
Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu Tyr Glu Ile
465                 470                 475                 480
Lys His Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile Ile Lys Ser
                485                 490                 495
Lys Glu Thr Thr Ile Thr Ala Glu Gly Leu Lys Pro Ala Ser Val Tyr
            500                 505                 510
Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly Val Phe Ser
        515                 520                 525
Arg Arg Phe Glu Phe Glu Thr Thr Pro Val Phe Ala Ala Ser Ser Asp
    530                 535                 540
Gln Ser Gln Ile Pro Val Ile Ala Val Ser Val Thr Val Gly Val Ile
545                 550                 555                 560
Leu Leu Ala Val Val Ile Gly Val Leu Leu Ser Gly Arg Arg Cys Gly
                565                 570                 575
Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met His Phe His
            580                 585                 590
Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile Asp Pro His
        595                 600                 605
Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala Lys Glu Ile
    610                 615                 620
Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala Gly Glu Phe
625                 630                 635                 640
Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Gly Lys Arg Glu Leu
                645                 650                 655
Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu Lys Gln Arg
            660                 665                 670
Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro
        675                 680                 685
Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser Lys Pro Val Met
```

```
    690                 695                 700
Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr Phe Leu Lys
705                 710                 715                 720
Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg
                725                 730                 735
Gly Ile Ser Ala Gly Met Lys Tyr Leu Ser Asp Met Gly Tyr Val His
            740                 745                 750
Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn Leu Val Cys
        755                 760                 765
Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro Glu
    770                 775                 780
Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala
785                 790                 795                 800
Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser Asp Val Trp
                805                 810                 815
Ser Tyr Gly Ile Val Met Trp Glu Val Val Ser Tyr Gly Glu Arg Pro
            820                 825                 830
Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val Glu Glu Gly
        835                 840                 845
Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu Tyr Gln Leu
    850                 855                 860
Met Leu Asp Cys Trp Gln Lys Glu Arg Asn Ser Arg Pro Lys Phe Asp
865                 870                 875                 880
Glu Ile Val Asn Met Leu Asp Lys Leu Ile Arg Asn Pro Ser Ser Leu
                885                 890                 895
Lys Thr Leu Val Asn Ala Ser Cys Arg Val Ser Asn Leu Leu Ala Glu
            900                 905                 910
His Ser Pro Leu Gly Ser Gly Ala Tyr Arg Ser Val Gly Glu Trp Leu
        915                 920                 925
Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe Met Glu Asn Gly
    930                 935                 940
Tyr Ser Ser Met Asp Ala Val Ala Gln Val Thr Leu Glu Asp Leu Arg
945                 950                 955                 960
Arg Leu Gly Val Thr Leu Val Gly His Gln Lys Lys Ile Met Asn Ser
                965                 970                 975
Leu Gln Glu Met Lys Val Gln Leu Val Asn Gly Met Val Pro Leu
            980                 985                 990


<210> 258
<211> 334
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. CAB63775
<309> 2005-01-20

<400> 258
Met Lys Asp Ser Pro Phe Gln Val Thr Lys Leu Tyr Trp Leu Asn Glu
 1               5                  10                  15
Lys Trp Asp Phe Ile Ala Ser Ala Ser Asp Met Ala Ala Glu Gln Gly
            20                  25                  30
Gln Ile Leu Val Ile Ala Thr Ala Ala Val Gly Gly Phe Thr Leu Leu
        35                  40                  45
Val Ile Leu Thr Leu Phe Phe Leu Ile Thr Gly Arg Cys Gln Trp Tyr
```

```
    50                  55                  60
Ile Lys Ala Lys Met Lys Ser Glu Glu Lys Arg Arg Asn His Leu Gln
65                  70                  75                  80
Asn Gly His Leu Arg Phe Pro Gly Ile Lys Thr Tyr Ile Asp Pro Asp
                85                  90                  95
Thr Tyr Glu Asp Pro Ser Leu Ala Val His Glu Phe Ala Lys Glu Ile
            100                 105                 110
Asp Pro Ser Arg Ile Arg Ile Glu Arg Val Ile Gly Ala Gly Glu Phe
        115                 120                 125
Gly Glu Val Cys Ser Gly Arg Leu Lys Thr Pro Gly Lys Arg Glu Ile
    130                 135                 140
Pro Val Ala Ile Lys Thr Leu Lys Gly Gly His Met Asp Arg Gln Arg
145                 150                 155                 160
Arg Asp Phe Leu Arg Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro
                165                 170                 175
Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Arg Ser Phe Pro Ala
            180                 185                 190
Ile Gly Val Glu Ala Phe Cys Pro Ser Phe Leu Arg Ala Gly Phe Leu
        195                 200                 205
Asn Ser Ile Gln Ala Pro His Pro Val Pro Gly Gly Gly Ser Leu Pro
    210                 215                 220
Pro Arg Ile Pro Ala Gly Arg Pro Val Met Ile Val Val Glu Tyr Met
225                 230                 235                 240
Glu Asn Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Gly His Phe
                245                 250                 255
Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met
            260                 265                 270
Lys Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg
        275                 280                 285
Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly
    290                 295                 300
Leu Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Thr
305                 310                 315                 320
Asp Leu Phe Gln Thr Leu Thr Leu Asn Leu Cys Tyr Ser Ala
                325                 330


<210> 259
<211> 998
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004431
<309> 2005-01-26

<400> 259
Met Val Phe Gln Thr Arg Tyr Pro Ser Trp Ile Ile Leu Cys Tyr Ile
 1               5                  10                  15
Trp Leu Leu Arg Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu
            20                  25                  30
Val Leu Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile
        35                  40                  45
Ser Ser Pro Pro Asn Gly Trp Glu Glu Ile Ser Gly Leu Asp Glu Asn
    50                  55                  60
Tyr Thr Pro Ile Arg Thr Tyr Gln Val Cys Gln Val Met Glu Pro Asn
```

65 70 75 80
Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Ser Lys Gly Asn Ala Gln
85 90 95
Arg Ile Phe Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu
100 105 110
Pro Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr
115 120 125
Glu Thr Asp Tyr Asp Thr Gly Arg Asn Ile Arg Glu Asn Leu Tyr Val
130 135 140
Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Gly Asp Leu
145 150 155 160
Gly Glu Arg Lys Met Lys Leu Asn Thr Glu Val Arg Glu Ile Gly Pro
165 170 175
Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys
180 185 190
Ile Ala Leu Val Ser Val Lys Val Tyr Tyr Lys Lys Cys Trp Ser Ile
195 200 205
Ile Glu Asn Leu Ala Ile Phe Pro Asp Thr Val Thr Gly Ser Glu Phe
210 215 220
Ser Ser Leu Val Glu Val Arg Gly Thr Cys Val Ser Ser Ala Glu Glu
225 230 235 240
Glu Ala Glu Asn Ala Pro Arg Met His Cys Ser Ala Glu Gly Glu Trp
245 250 255
Leu Val Pro Ile Gly Lys Cys Ile Cys Lys Ala Gly Tyr Gln Gln Lys
260 265 270
Gly Asp Thr Cys Glu Pro Cys Gly Arg Gly Phe Tyr Lys Ser Ser Ser
275 280 285
Gln Asp Leu Gln Cys Ser Arg Cys Pro Thr His Ser Phe Ser Asp Lys
290 295 300
Glu Gly Ser Ser Arg Cys Glu Cys Glu Asp Gly Tyr Tyr Arg Ala Pro
305 310 315 320
Ser Asp Pro Pro Tyr Val Ala Cys Thr Arg Pro Pro Ser Ala Pro Gln
325 330 335
Asn Leu Ile Phe Asn Ile Asn Gln Thr Thr Val Ser Leu Glu Trp Ser
340 345 350
Pro Pro Ala Asp Asn Gly Gly Arg Asn Asp Val Thr Tyr Arg Ile Leu
355 360 365
Cys Lys Arg Cys Ser Trp Glu Gln Gly Glu Cys Val Pro Cys Gly Ser
370 375 380
Asn Ile Gly Tyr Met Pro Gln Gln Thr Gly Leu Glu Asp Asn Tyr Val
385 390 395 400
Thr Val Met Asp Leu Leu Ala His Ala Asn Tyr Thr Phe Glu Val Glu
405 410 415
Ala Val Asn Gly Val Ser Asp Leu Ser Arg Ser Gln Arg Leu Phe Ala
420 425 430
Ala Val Ser Ile Thr Thr Gly Gln Ala Ala Pro Ser Gln Val Ser Gly
435 440 445
Val Met Lys Glu Arg Val Leu Gln Arg Ser Val Glu Leu Ser Trp Gln
450 455 460
Glu Pro Glu His Pro Asn Gly Val Ile Thr Glu Tyr Glu Ile Lys Tyr
465 470 475 480
Tyr Glu Lys Asp Gln Arg Glu Arg Thr Tyr Ser Thr Val Lys Thr Lys
485 490 495
Ser Thr Ser Ala Ser Ile Asn Asn Leu Lys Pro Gly Thr Val Tyr Val
500 505 510
Phe Gln Ile Arg Ala Phe Thr Ala Ala Gly Tyr Gly Asn Tyr Ser Pro

```
        515                 520                 525
Arg Leu Asp Val Ala Thr Leu Glu Glu Ala Thr Gly Lys Met Phe Glu
    530                 535                 540
Ala Thr Ala Val Ser Ser Glu Gln Asn Pro Val Ile Ile Ile Ala Val
545                 550                 555                 560
Val Ala Val Ala Gly Thr Ile Ile Leu Val Phe Met Val Phe Gly Phe
                565                 570                 575
Ile Ile Gly Arg Arg His Cys Gly Tyr Ser Lys Ala Asp Gln Glu Gly
            580                 585                 590
Asp Glu Glu Leu Tyr Phe His Phe Lys Phe Pro Gly Thr Lys Thr Tyr
        595                 600                 605
Ile Asp Pro Glu Thr Tyr Glu Asp Pro Asn Arg Ala Val His Gln Phe
    610                 615                 620
Ala Lys Glu Leu Asp Ala Ser Cys Ile Lys Ile Glu Arg Val Ile Gly
625                 630                 635                 640
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Gly
                645                 650                 655
Lys Arg Asp Val Ala Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670
Glu Lys Gln Arg Arg Asp Phe Leu Cys Glu Ala Ser Ile Met Gly Gln
        675                 680                 685
Phe Asp His Pro Asn Val Val His Leu Glu Gly Val Val Thr Arg Gly
    690                 695                 700
Lys Pro Val Met Ile Val Ile Glu Phe Met Glu Asn Gly Ala Leu Asp
705                 710                 715                 720
Ala Phe Leu Arg Lys His Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg Tyr Leu Ala Asp Met
            740                 745                 750
Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Ile Glu
    770                 775                 780
Asp Asp Pro Glu Ala Val Tyr Thr Thr Thr Gly Gly Lys Ile Pro Val
785                 790                 795                 800
Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala
                805                 810                 815
Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr
            820                 825                 830
Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala
        835                 840                 845
Ile Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Asp Cys Pro Ala Gly
    850                 855                 860
Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Glu Arg Ala Glu Arg
865                 870                 875                 880
Pro Lys Phe Glu Gln Ile Val Gly Ile Leu Asp Lys Met Ile Arg Asn
                885                 890                 895
Pro Asn Ser Leu Lys Thr Pro Leu Gly Thr Cys Ser Arg Pro Ile Ser
            900                 905                 910
Pro Leu Leu Asp Gln Asn Thr Pro Asp Phe Thr Thr Phe Cys Ser Val
        915                 920                 925
Gly Glu Trp Leu Gln Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe
    930                 935                 940
Thr Ala Ala Gly Tyr Asn Ser Leu Glu Ser Val Ala Arg Met Thr Ile
945                 950                 955                 960
Glu Asp Val Met Ser Leu Gly Ile Thr Leu Val Gly His Gln Lys Lys
```

```
                965                 970                 975
Ile Met Ser Ser Ile Gln Thr Met Arg Ala Gln Met Leu His Leu His
            980                 985                 990
Gly Thr Gly Ile Gln Val
        995


<210> 260
<211> 1005
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP065387
<309> 2004-11-16

<400> 260
Met Ala Pro Ala Arg Gly Arg Leu Pro Pro Ala Leu Trp Val Val Thr
 1               5                  10                  15
Ala Ala Ala Ala Ala Ala Thr Cys Val Ser Ala Ala Arg Gly Glu Val
            20                  25                  30
Asn Leu Leu Asp Thr Ser Thr Ile His Gly Asp Trp Gly Trp Leu Thr
        35                  40                  45
Tyr Pro Ala His Gly Trp Asp Ser Ile Asn Glu Val Asp Glu Ser Phe
    50                  55                  60
Gln Pro Ile His Thr Tyr Gln Val Cys Asn Val Met Ser Pro Asn Gln
65                  70                  75                  80
Asn Asn Trp Leu Arg Thr Ser Trp Val Pro Arg Asp Gly Ala Arg Arg
                85                  90                  95
Val Tyr Ala Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Met Pro
            100                 105                 110
Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Leu Glu
        115                 120                 125
Ser Asp Arg Asp Leu Gly Ala Ser Thr Gln Glu Ser Gln Phe Leu Lys
    130                 135                 140
Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gly Ala Asp Leu Gly
145                 150                 155                 160
Val Arg Arg Leu Lys Leu Asn Thr Glu Val Arg Ser Val Gly Pro Leu
                165                 170                 175
Ser Lys Arg Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Leu
            180                 185                 190
Ala Ile Leu Ser Leu Arg Ile Tyr Tyr Lys Lys Cys Pro Ala Met Val
        195                 200                 205
Arg Asn Leu Ala Ala Phe Ser Glu Ala Val Thr Gly Ala Asp Ser Ser
    210                 215                 220
Ser Leu Val Glu Val Arg Gly Gln Cys Val Arg His Ser Glu Glu Arg
225                 230                 235                 240
Asp Thr Pro Lys Met Tyr Cys Ser Ala Glu Gly Glu Trp Leu Val Pro
                245                 250                 255
Ile Gly Lys Cys Val Cys Ser Ala Gly Tyr Glu Glu Arg Arg Asp Ala
            260                 265                 270
Cys Val Ala Cys Glu Leu Gly Phe Tyr Lys Ser Ala Pro Gly Asp Gln
        275                 280                 285
Leu Cys Ala Arg Cys Pro Pro His Ser His Ser Ala Ala Pro Ala Ala
    290                 295                 300
Gln Ala Cys His Cys Asp Leu Ser Tyr Tyr Arg Ala Ala Leu Asp Pro
```

```
305                 310                 315                 320
Pro Ser Ser Ala Cys Thr Arg Pro Pro Ser Ala Pro Val Asn Leu Ile
                325                 330                 335
Ser Ser Val Asn Gly Thr Ser Val Thr Leu Glu Trp Ala Pro Pro Leu
            340                 345                 350
Asp Pro Gly Gly Arg Ser Asp Ile Thr Tyr Asn Ala Val Cys Arg Arg
        355                 360                 365
Cys Pro Trp Ala Leu Ser Arg Cys Glu Ala Cys Gly Ser Gly Thr Arg
    370                 375                 380
Phe Val Pro Gln Gln Thr Ser Leu Val Gln Ala Ser Leu Leu Val Ala
385                 390                 395                 400
Asn Leu Leu Ala His Met Asn Tyr Ser Phe Trp Ile Glu Ala Val Asn
                405                 410                 415
Gly Val Ser Asp Leu Ser Pro Glu Pro Arg Arg Ala Ala Val Val Asn
            420                 425                 430
Ile Thr Thr Asn Gln Ala Ala Pro Ser Gln Val Val Val Ile Arg Gln
        435                 440                 445
Glu Arg Ala Gly Gln Thr Ser Val Ser Leu Leu Trp Gln Glu Pro Glu
    450                 455                 460
Gln Pro Asn Gly Ile Ile Leu Glu Tyr Glu Ile Lys Tyr Tyr Glu Lys
465                 470                 475                 480
Asp Lys Glu Met Gln Ser Tyr Ser Thr Leu Lys Ala Val Thr Thr Arg
                485                 490                 495
Ala Thr Val Ser Gly Leu Lys Pro Gly Thr Arg Tyr Val Phe Gln Val
            500                 505                 510
Arg Ala Arg Thr Ser Ala Gly Cys Gly Arg Phe Ser Gln Ala Met Glu
        515                 520                 525
Val Glu Thr Gly Lys Pro Arg Pro Arg Tyr Asp Thr Arg Thr Ile Val
    530                 535                 540
Trp Ile Cys Leu Thr Leu Ile Thr Gly Leu Val Val Leu Leu Leu Leu
545                 550                 555                 560
Leu Ile Cys Lys Lys Arg His Cys Gly Tyr Ser Lys Ala Phe Gln Asp
                565                 570                 575
Ser Asp Glu Glu Lys Met His Tyr Gln Asn Gly Gln Ala Pro Pro Pro
            580                 585                 590
Val Phe Leu Pro Leu His His Pro Pro Gly Lys Leu Pro Glu Pro Gln
        595                 600                 605
Phe Tyr Ala Glu Pro His Thr Tyr Glu Glu Pro Gly Arg Ala Gly Arg
    610                 615                 620
Ser Phe Thr Arg Glu Ile Glu Ala Ser Arg Ile His Ile Glu Lys Ile
625                 630                 635                 640
Ile Gly Ser Gly Asp Ser Gly Glu Val Cys Tyr Gly Arg Leu Arg Val
                645                 650                 655
Pro Gly Gln Arg Asp Val Pro Val Ala Ile Lys Ala Leu Lys Ala Gly
            660                 665                 670
Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met
        675                 680                 685
Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
    690                 695                 700
Arg Gly Arg Leu Ala Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser
705                 710                 715                 720
Leu Asp Thr Phe Leu Arg Thr His Asp Gly Gln Phe Thr Ile Met Gln
                725                 730                 735
Leu Val Gly Met Leu Arg Gly Val Gly Ala Gly Met Arg Tyr Leu Ser
            740                 745                 750
Asp Leu Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val
```

```
        755                 760                 765
Asp Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val
    770                 775                 780
Leu Glu Asp Asp Pro Asp Ala Ala Tyr Thr Thr Thr Gly Gly Lys Ile
785                 790                 795                 800
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Thr Phe Ser
                805                 810                 815
Ser Ala Ser Asp Val Trp Ser Phe Gly Val Val Met Trp Glu Val Leu
            820                 825                 830
Ala Tyr Gly Glu Arg Pro Tyr Trp Asn Met Thr Asn Arg Asp Val Ile
        835                 840                 845
Ser Ser Val Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Gly Cys Pro
    850                 855                 860
His Ala Leu His Gln Leu Met Leu Asp Cys Trp His Lys Asp Arg Ala
865                 870                 875                 880
Gln Arg Pro Arg Phe Ser Gln Ile Val Ser Val Leu Asp Ala Leu Ile
                885                 890                 895
Arg Ser Pro Glu Ser Leu Arg Ala Thr Ala Thr Val Ser Arg Cys Pro
            900                 905                 910
Pro Pro Ala Phe Val Arg Ser Cys Phe Asp Leu Arg Gly Gly Ser Gly
        915                 920                 925
Gly Gly Gly Gly Leu Thr Val Gly Asp Trp Leu Asp Ser Ile Arg Met
    930                 935                 940
Gly Arg Tyr Arg Asp His Phe Ala Ala Gly Gly Tyr Ser Ser Leu Gly
945                 950                 955                 960
Met Val Leu Arg Met Asn Ala Gln Asp Val Arg Ala Leu Gly Ile Thr
                965                 970                 975
Leu Met Gly His Gln Lys Lys Ile Leu Gly Ser Ile Gln Thr Met Arg
            980                 985                 990
Ala Gln Leu Thr Ser Thr Gln Gly Pro Arg Arg His Leu
        995                 1000                1005


<210> 261
<211> 984
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004432
<309> 2004-11-15

<400> 261
Met Ala Leu Asp Tyr Leu Leu Leu Leu Leu Leu Ala Ser Ala Val Ala
 1               5                  10                  15
Ala Met Glu Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu
            20                  25                  30
Gly Trp Thr Ala Asn Pro Ala Ser Gly Trp Glu Glu Val Ser Gly Tyr
        35                  40                  45
Asp Glu Asn Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe
    50                  55                  60
Glu Pro Asn Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg
65                  70                  75                  80
Gly Ala His Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys
                85                  90                  95
Ser Ser Leu Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu
```

```
                100                 105                 110
Tyr Tyr Tyr Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe
        115                 120                 125
Trp Ser Glu Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu
    130                 135                 140
Ser Phe Ser Gln Val Asp Phe Gly Gly Arg Leu Met Lys Val Asn Thr
145                 150                 155                 160
Glu Val Arg Ser Phe Gly Pro Leu Thr Arg Asn Gly Phe Tyr Leu Ala
                165                 170                 175
Phe Gln Asp Tyr Gly Ala Cys Met Ser Leu Leu Ser Val Arg Val Phe
            180                 185                 190
Phe Lys Lys Cys Pro Ser Ile Val Gln Asn Phe Ala Val Phe Pro Glu
        195                 200                 205
Thr Met Thr Gly Ala Glu Ser Thr Ser Leu Val Ile Ala Arg Gly Thr
    210                 215                 220
Cys Ile Pro Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys
225                 230                 235                 240
Asn Gly Asp Gly Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys
                245                 250                 255
Pro Gly Tyr Glu Pro Glu Asn Ser Val Ala Cys Lys Ala Cys Pro Ala
            260                 265                 270
Gly Thr Phe Lys Ala Ser Gln Glu Ala Glu Gly Cys Ser His Cys Pro
        275                 280                 285
Ser Asn Ser Arg Ser Pro Ala Glu Ala Ser Pro Ile Cys Thr Cys Arg
    290                 295                 300
Thr Gly Tyr Tyr Arg Ala Asp Phe Asp Pro Pro Glu Val Ala Cys Thr
305                 310                 315                 320
Ser Val Pro Ser Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr
                325                 330                 335
Ser Ile Ile Leu Glu Trp His Pro Pro Arg Glu Thr Gly Gly Arg Asp
            340                 345                 350
Asp Val Thr Tyr Asn Ile Ile Cys Lys Lys Cys Arg Ala Asp Arg Arg
        355                 360                 365
Ser Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu
    370                 375                 380
Gly Leu Thr Glu Cys Arg Val Ser Ile Ser Ser Leu Trp Ala His Thr
385                 390                 395                 400
Pro Tyr Thr Phe Asp Ile Gln Ala Ile Asn Gly Val Ser Ser Lys Ser
                405                 410                 415
Pro Phe Pro Pro Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala
            420                 425                 430
Ala Pro Ser Thr Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg
        435                 440                 445
Ser Ile Thr Leu Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile
    450                 455                 460
Leu Asp Tyr Glu Ile Arg Tyr Tyr Glu Lys Glu His Asn Glu Phe Asn
465                 470                 475                 480
Ser Ser Met Ala Arg Ser Gln Thr Asn Thr Ala Arg Ile Asp Gly Leu
                485                 490                 495
Arg Pro Gly Met Val Tyr Val Val Gln Val Arg Ala Arg Thr Val Ala
            500                 505                 510
Gly Tyr Gly Lys Phe Ser Gly Lys Met Cys Phe Gln Thr Leu Thr Asp
        515                 520                 525
Asp Asp Tyr Lys Ser Glu Leu Arg Glu Gln Leu Pro Leu Ile Ala Gly
    530                 535                 540
Ser Ala Ala Ala Gly Val Val Phe Val Val Ser Leu Val Ala Ile Ser
```

```
545                 550                 555                 560
Ile Val Cys Ser Arg Lys Arg Ala Tyr Ser Lys Glu Ala Val Tyr Ser
                565                 570                 575
Asp Lys Leu Gln His Tyr Ser Thr Gly Arg Gly Ser Pro Gly Met Lys
            580                 585                 590
Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg
        595                 600                 605
Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Val Lys Ile Glu Glu Val
    610                 615                 620
Ile Gly Ala Gly Glu Phe Gly Glu Val Tyr Lys Gly Arg Leu Lys Leu
625                 630                 635                 640
Pro Gly Lys Arg Glu Ile Tyr Val Ala Ile Lys Thr Leu Lys Ala Gly
                645                 650                 655
Tyr Ser Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met
            660                 665                 670
Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
        675                 680                 685
Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ala
    690                 695                 700
Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln
705                 710                 715                 720
Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala
                725                 730                 735
Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val
            740                 745                 750
Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Tyr
        755                 760                 765
Leu Gln Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly
    770                 775                 780
Lys Ile Pro Val Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu
                805                 810                 815
Val Met Ser Phe Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830
Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845
Cys Pro Ala Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860
Arg Asn Ser Arg Pro Arg Phe Ala Glu Ile Val Asn Thr Leu Asp Lys
865                 870                 875                 880
Met Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr Ala
                885                 890                 895
Val Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr Ala
            900                 905                 910
Phe Thr Thr Val Asp Asp Trp Leu Ser Ala Ile Lys Met Val Gln Tyr
        915                 920                 925
Arg Asp Ser Phe Leu Thr Ala Gly Phe Thr Ser Leu Gln Leu Val Thr
    930                 935                 940
Gln Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Ile Thr Leu Ala Gly
945                 950                 955                 960
His Gln Lys Lys Ile Leu Asn Ser Ile His Ser Met Arg Val Gln Ile
                965                 970                 975
Ser Gln Ser Pro Thr Ala Met Ala
            980
```

<210> 262
<211> 1055
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. AAB94602
<309> 2000-11-29

<400> 262

```
Met Ala Leu Arg Arg Leu Gly Ala Ala Leu Leu Leu Leu Pro Leu Leu
 1               5                  10                  15
Ala Ala Val Glu Glu Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu
            20                  25                  30
Leu Gly Trp Met Val His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly
        35                  40                  45
Tyr Asp Glu Asn Met Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val
    50                  55                  60
Phe Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Lys Phe Ile Arg Arg
65                  70                  75                  80
Arg Gly Ala His Arg Ile His Val Glu Met Lys Phe Ser Val Arg Asp
                85                  90                  95
Cys Ser Ser Ile Pro Ser Val Pro Gly Ser Cys Lys Glu Thr Phe Asn
            100                 105                 110
Leu Tyr Tyr Tyr Glu Ala Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro
        115                 120                 125
Asn Trp Met Glu Asn Pro Trp Val Lys Val Asp Thr Ile Ala Ala Asp
    130                 135                 140
Glu Ser Phe Ser Gln Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn
145                 150                 155                 160
Thr Glu Val Arg Ser Phe Gly Pro Val Ser Arg Ser Gly Phe Tyr Leu
                165                 170                 175
Ala Phe Gln Asp Tyr Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val
            180                 185                 190
Phe Tyr Arg Lys Cys Pro Arg Ile Ile Gln Asn Gly Ala Ile Phe Gln
        195                 200                 205
Glu Thr Leu Ser Gly Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly
    210                 215                 220
Ser Cys Ile Ala Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr
225                 230                 235                 240
Cys Asn Gly Asp Gly Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys
                245                 250                 255
Lys Ala Gly Phe Glu Ala Val Glu Asn Gly Thr Val Cys Arg Gly Cys
            260                 265                 270
Pro Ser Gly Thr Phe Lys Ala Asn Gln Gly Asp Glu Ala Cys Thr His
        275                 280                 285
Cys Pro Ile Asn Ser Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val
    290                 295                 300
Cys Arg Asn Gly Tyr Tyr Arg Ala Asp Leu Asp Pro Leu Asp Met Pro
305                 310                 315                 320
Cys Thr Thr Ile Pro Ser Ala Pro Gln Ala Val Ile Ser Ser Val Asn
                325                 330                 335
Glu Thr Ser Leu Met Leu Glu Trp Thr Pro Pro Arg Asp Ser Gly Gly
            340                 345                 350
Arg Glu Asp Leu Val Tyr Asn Ile Ile Cys Lys Ser Cys Gly Ser Gly
```

```
        355                 360                 365
Arg Gly Ala Cys Thr Arg Cys Gly Asp Asn Val Gln Tyr Ala Pro Arg
    370                 375                 380
Gln Leu Gly Leu Thr Glu Pro Arg Ile Tyr Ile Ser Asp Leu Leu Ala
385                 390                 395                 400
His Thr Gln Tyr Thr Phe Glu Ile Gln Ala Val Asn Gly Val Thr Asp
                405                 410                 415
Gln Ser Pro Phe Ser Pro Gln Phe Ala Ser Val Asn Ile Thr Thr Asn
            420                 425                 430
Gln Ala Ala Pro Ser Ala Val Ser Ile Met His Gln Val Ser Arg Thr
        435                 440                 445
Val Asp Ser Ile Thr Leu Ser Trp Ser Gln Pro Asp Gln Pro Asn Gly
    450                 455                 460
Val Ile Leu Asp Tyr Glu Leu Gln Tyr Tyr Glu Lys Glu Leu Ser Glu
465                 470                 475                 480
Tyr Asn Ala Thr Ala Ile Lys Ser Pro Thr Asn Thr Val Thr Val Gln
                485                 490                 495
Gly Leu Lys Ala Gly Ala Ile Tyr Val Phe Gln Val Arg Ala Arg Thr
            500                 505                 510
Val Ala Gly Tyr Gly Arg Tyr Ser Gly Lys Met Tyr Phe Gln Thr Met
        515                 520                 525
Thr Glu Ala Glu Tyr Gln Thr Ser Ile Gln Glu Lys Leu Pro Leu Ile
    530                 535                 540
Ile Gly Ser Ser Ala Ala Gly Leu Val Phe Leu Ile Ala Val Val Val
545                 550                 555                 560
Ile Ala Ile Val Cys Asn Arg Arg Gly Phe Glu Arg Ala Asp Ser Glu
                565                 570                 575
Tyr Thr Asp Lys Leu Gln His Tyr Thr Ser Gly His Met Thr Pro Gly
            580                 585                 590
Met Lys Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala
        595                 600                 605
Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val Lys Ile Glu
    610                 615                 620
Gln Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly His Leu
625                 630                 635                 640
Lys Leu Pro Gly Lys Arg Glu Ile Phe Val Ala Ile Lys Thr Leu Lys
                645                 650                 655
Ser Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
            660                 665                 670
Ile Met Gly Gln Phe Asp His Pro Asn Val Ile His Leu Glu Gly Val
        675                 680                 685
Val Thr Lys Ser Thr Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn
    690                 695                 700
Gly Ser Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val
705                 710                 715                 720
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr
                725                 730                 735
Leu Ala Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750
Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765
Arg Phe Leu Glu Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ala Leu
    770                 775                 780
Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr
785                 790                 795                 800
Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met
```

```
                805                 810                 815
Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn
            820                 825                 830
Gln Asp Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro
        835                 840                 845
Met Asp Cys Pro Ser Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln
    850                 855                 860
Lys Asp Arg Asn His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu
865                 870                 875                 880
Asp Lys Met Ile Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu
                885                 890                 895
Ser Ser Gly Ile Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr
            900                 905                 910
Thr Ser Phe Asn Thr Val Asp Glu Trp Leu Glu Ala Ile Lys Met Gly
        915                 920                 925
Gln Tyr Lys Glu Ser Phe Ala Asn Ala Gly Phe Thr Ser Phe Asp Val
    930                 935                 940
Val Ser Gln Met Met Met Glu Asp Ile Leu Arg Val Gly Val Thr Leu
945                 950                 955                 960
Ala Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala
                965                 970                 975
Gln Met Asn Gln Ile Gln Ser Val Glu Gly Gln Pro Leu Ala Arg Arg
            980                 985                 990
Pro Arg Ala Thr Gly Arg Thr Lys Arg Cys Gln Pro Arg Asp Val Thr
        995                 1000                1005
Lys Lys Thr Cys Asn Ser Asn Asp Gly Lys Lys Lys Gly Met Gly Lys
    1010                1015                1020
Lys Lys Thr Asp Pro Gly Arg Gly Arg Glu Ile Gln Gly Ile Phe Phe
1025                1030                1035                1040
Lys Glu Asp Ser His Lys Glu Ser Asn Asp Cys Ser Cys Gly Gly
                1045                1050                1055
```

<210> 263
<211> 998
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004434
<309> 2004-11-16

<400> 263

```
Met Ala Arg Ala Arg Pro Pro Pro Pro Pro Ser Pro Pro Pro Gly Leu
 1               5                  10                  15
Leu Pro Leu Leu Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Pro
            20                  25                  30
Ala Gly Cys Arg Ala Leu Glu Glu Thr Leu Met Asp Thr Lys Trp Val
        35                  40                  45
Thr Ser Glu Leu Ala Trp Thr Ser His Pro Glu Ser Gly Trp Glu Glu
    50                  55                  60
Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg Thr Tyr Gln Val
65                  70                  75                  80
Cys Asn Val Arg Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Gly Phe
                85                  90                  95
Ile Trp Arg Arg Asp Val Gln Arg Val Tyr Val Glu Leu Lys Phe Thr
```

```
                100                 105                 110
Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly Ser Cys Lys Glu
        115                 120                 125
Thr Phe Asn Leu Phe Tyr Tyr Glu Ala Asp Ser Asp Val Ala Ser Ala
    130                 135                 140
Ser Ser Pro Phe Trp Met Glu Asn Pro Tyr Val Lys Val Asp Thr Ile
145                 150                 155                 160
Ala Pro Asp Glu Ser Phe Ser Arg Leu Asp Ala Gly Arg Val Asn Thr
                165                 170                 175
Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu Ala
            180                 185                 190
Phe Gln Asp Gln Gly Ala Cys Met Ser Leu Ile Ser Val Arg Ala Phe
        195                 200                 205
Tyr Lys Lys Cys Ala Ser Thr Thr Ala Gly Phe Ala Leu Phe Pro Glu
    210                 215                 220
Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile Ala Pro Gly Thr
225                 230                 235                 240
Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu Lys Leu Tyr Cys
                245                 250                 255
Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala Cys Thr Cys Ala
            260                 265                 270
Thr Gly His Glu Pro Ala Ala Lys Glu Ser Gln Cys Arg Pro Cys Pro
        275                 280                 285
Pro Gly Ser Tyr Lys Ala Lys Gln Gly Glu Gly Pro Cys Leu Pro Cys
    290                 295                 300
Pro Pro Asn Ser Arg Thr Thr Ser Pro Ala Ala Ser Ile Cys Thr Cys
305                 310                 315                 320
His Asn Asn Phe Tyr Arg Ala Asp Ser Asp Ser Ala Asp Ser Ala Cys
                325                 330                 335
Thr Thr Val Pro Ser Pro Pro Arg Gly Val Ile Ser Asn Val Asn Glu
            340                 345                 350
Thr Ser Leu Ile Leu Glu Trp Ser Glu Pro Arg Asp Leu Gly Gly Arg
        355                 360                 365
Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys His Gly Ala Gly
    370                 375                 380
Gly Ala Ser Ala Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro
385                 390                 395                 400
Arg Gln Leu Gly Leu Thr Glu Arg Arg Val His Ile Ser His Leu Leu
                405                 410                 415
Ala His Thr Arg Tyr Thr Phe Glu Val Gln Ala Val Asn Gly Val Ser
            420                 425                 430
Gly Lys Ser Pro Leu Pro Pro Arg Tyr Ala Ala Val Asn Ile Thr Thr
        435                 440                 445
Asn Gln Ala Ala Pro Ser Glu Val Pro Thr Leu Arg Leu His Ser Ser
    450                 455                 460
Ser Gly Ser Ser Leu Thr Leu Ser Trp Ala Pro Pro Glu Arg Pro Asn
465                 470                 475                 480
Gly Val Ile Leu Asp Tyr Glu Met Lys Tyr Phe Glu Lys Ser Glu Gly
                485                 490                 495
Ile Ala Ser Thr Val Thr Ser Gln Met Asn Ser Val Gln Leu Asp Gly
            500                 505                 510
Leu Arg Pro Asp Ala Arg Tyr Val Val Gln Val Arg Ala Arg Thr Val
        515                 520                 525
Ala Gly Tyr Gly Gln Tyr Ser Arg Pro Ala Glu Phe Glu Thr Thr Ser
    530                 535                 540
Glu Arg Gly Ser Gly Ala Gln Gln Leu Gln Glu Gln Leu Pro Leu Ile
```

```
545                 550                 555                 560
Val Gly Ser Ala Thr Ala Gly Leu Val Phe Val Val Ala Val Val Val
                565                 570                 575
Ile Ala Ile Val Cys Leu Arg Lys Gln Arg His Gly Ser Asp Ser Glu
            580                 585                 590
Tyr Thr Glu Lys Leu Gln Gln Tyr Ile Ala Pro Gly Met Lys Val Tyr
        595                 600                 605
Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe
    610                 615                 620
Ala Lys Glu Ile Asp Val Ser Cys Val Lys Ile Glu Glu Val Ile Gly
625                 630                 635                 640
Ala Gly Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Gln Pro Gly
                645                 650                 655
Arg Arg Glu Val Phe Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670
Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln
        675                 680                 685
Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Ser
    690                 695                 700
Arg Pro Val Met Ile Leu Thr Glu Phe Met Glu Asn Cys Ala Leu Asp
705                 710                 715                 720
Ser Phe Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ser Glu Met
            740                 745                 750
Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu
    770                 775                 780
Asp Asp Pro Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile
785                 790                 795                 800
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr
                805                 810                 815
Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met
            820                 825                 830
Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile
        835                 840                 845
Asn Ala Val Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro
    850                 855                 860
Thr Ala Leu His Gln Leu Met Leu Asp Cys Trp Val Arg Asp Arg Asn
865                 870                 875                 880
Leu Arg Pro Lys Phe Ser Gln Ile Val Asn Thr Leu Asp Lys Leu Ile
                885                 890                 895
Arg Asn Ala Ala Ser Leu Lys Val Ile Ala Ser Ala Gln Ser Gly Met
            900                 905                 910
Ser Gln Pro Leu Leu Asp Arg Thr Val Pro Asp Tyr Thr Thr Phe Thr
        915                 920                 925
Thr Val Gly Asp Trp Leu Asp Ala Ile Lys Met Gly Arg Tyr Lys Glu
    930                 935                 940
Ser Phe Val Ser Ala Gly Phe Ala Ser Phe Asp Leu Val Ala Gln Met
945                 950                 955                 960
Thr Ala Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln
                965                 970                 975
Lys Lys Ile Leu Ser Ser Ile Gln Asp Met Arg Leu Gln Met Asn Gln
            980                 985                 990
Thr Leu Pro Val Gln Val
```

995

<210> 264
<211> 987
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No.NP004435
<309> 2004-11-16

<400> 264
Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
1 5 10 15
Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
20 25 30
Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
35 40 45
Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
50 55 60
Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65 70 75 80
Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
85 90 95
Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
100 105 110
Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
115 120 125
Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
130 135 140
His Leu Thr Arg Lys Arg Pro Gly Ala Glu Ala Thr Gly Lys Val Asn
145 150 155 160
Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
165 170 175
Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
180 185 190
Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
195 200 205
Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
210 215 220
Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225 230 235 240
Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
245 250 255
Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Ala Cys Ala
260 265 270
Gln Gly Thr Phe Lys Pro Leu Ser Gly Glu Gly Ser Cys Gln Pro Cys
275 280 285
Pro Ala Asn Ser His Ser Asn Thr Ile Gly Ser Ala Val Cys Gln Cys
290 295 300
Arg Val Gly Tyr Phe Arg Ala Arg Thr Asp Pro Arg Gly Ala Pro Cys
305 310 315 320
Thr Thr Pro Pro Ser Ala Pro Arg Ser Val Val Ser Arg Leu Asn Gly
325 330 335
Ser Ser Leu His Leu Glu Trp Ser Ala Pro Leu Glu Ser Gly Gly Arg

```
            340                 345                 350
Glu Asp Leu Thr Tyr Ala Leu Arg Cys Arg Glu Cys Arg Pro Gly Gly
        355                 360                 365
Ser Cys Ala Pro Cys Gly Gly Asp Leu Thr Phe Asp Pro Gly Pro Arg
    370                 375                 380
Asp Leu Val Glu Pro Trp Val Val Val Arg Gly Leu Arg Pro Asp Phe
385                 390                 395                 400
Thr Tyr Thr Phe Glu Val Thr Ala Leu Asn Gly Val Ser Ser Leu Ala
                405                 410                 415
Thr Gly Pro Val Pro Phe Glu Pro Val Asn Val Thr Thr Asp Arg Glu
            420                 425                 430
Val Pro Pro Ala Val Ser Asp Ile Arg Val Thr Arg Ser Ser Pro Ser
        435                 440                 445
Ser Leu Ser Leu Ala Trp Ala Val Pro Arg Ala Pro Ser Gly Ala Val
    450                 455                 460
Leu Asp Tyr Glu Val Lys Tyr His Glu Lys Gly Ala Glu Gly Pro Ser
465                 470                 475                 480
Ser Val Arg Phe Leu Lys Thr Ser Glu Asn Arg Ala Glu Leu Arg Gly
                485                 490                 495
Leu Lys Arg Gly Ala Ser Tyr Leu Val Gln Val Arg Ala Arg Ser Glu
            500                 505                 510
Ala Gly Tyr Gly Pro Phe Gly Gln Glu His His Ser Gln Thr Gln Leu
        515                 520                 525
Asp Glu Ser Glu Gly Trp Arg Glu Gln Leu Ala Leu Ile Ala Gly Thr
    530                 535                 540
Ala Val Val Gly Val Val Leu Val Leu Val Val Ile Val Val Ala Val
545                 550                 555                 560
Leu Cys Leu Arg Lys Gln Ser Asn Gly Arg Glu Ala Glu Tyr Ser Asp
                565                 570                 575
Lys His Gly Gln Tyr Leu Ile Gly His Gly Thr Lys Val Tyr Ile Asp
            580                 585                 590
Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys
        595                 600                 605
Glu Ile Asp Val Ser Tyr Val Lys Ile Glu Glu Val Ile Gly Ala Gly
    610                 615                 620
Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Ala Pro Gly Lys Lys
625                 630                 635                 640
Glu Ser Cys Val Ala Ile Lys Thr Leu Lys Gly Gly Tyr Thr Glu Arg
                645                 650                 655
Gln Arg Arg Glu Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Glu
            660                 665                 670
His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Asn Ser Met Pro
        675                 680                 685
Val Met Ile Leu Thr Glu Phe Met Glu Asn Gly Ala Leu Asp Ser Phe
    690                 695                 700
Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met
705                 710                 715                 720
Leu Arg Gly Ile Ala Ser Gly Met Arg Tyr Leu Ala Glu Met Ser Tyr
                725                 730                 735
Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu
            740                 745                 750
Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Glu Asn
        755                 760                 765
Ser Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile Pro Ile
    770                 775                 780
Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala
```

```
785                 790                 795                 800
Ser Asp Ala Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Phe
                805                 810                 815
Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Asn Ala
            820                 825                 830
Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Pro Asp Cys Pro Thr Ser
        835                 840                 845
Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ala Arg
    850                 855                 860
Pro Arg Phe Pro Gln Val Val Ser Ala Leu Asp Lys Met Ile Arg Asn
865                 870                 875                 880
Pro Ala Ser Leu Lys Ile Val Ala Arg Glu Asn Gly Gly Ala Ser His
                885                 890                 895
Pro Leu Leu Asp Gln Arg Gln Pro His Tyr Ser Ala Phe Gly Ser Val
            900                 905                 910
Gly Glu Trp Leu Arg Ala Ile Lys Met Gly Arg Tyr Glu Glu Ser Phe
        915                 920                 925
Ala Ala Ala Gly Phe Gly Ser Phe Glu Leu Val Ser Gln Ile Ser Ala
    930                 935                 940
Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln Lys Lys
945                 950                 955                 960
Ile Leu Ala Ser Val Gln His Met Lys Ser Gln Ala Lys Pro Gly Thr
                965                 970                 975
Pro Gly Gly Thr Gly Gly Pro Ala Pro Gln Tyr
            980                 985
```

<210> 265
<211> 1006
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No.NP004436
<309> 2004-11-29

<400> 265

```
Met Val Cys Ser Leu Trp Val Leu Leu Leu Val Ser Ser Val Leu Ala
 1               5                  10                  15
Leu Glu Glu Val Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly
            20                  25                  30
Trp Leu Thr Tyr Pro Pro Gly Gly Trp Asp Glu Val Ser Val Leu Asp
        35                  40                  45
Asp Gln Arg Arg Leu Thr Arg Thr Phe Glu Ala Cys His Val Ala Gly
    50                  55                  60
Ala Pro Pro Gly Thr Gly Gln Asp Asn Trp Leu Gln Thr His Phe Val
65                  70                  75                  80
Glu Arg Arg Gly Ala Gln Arg Ala His Ile Arg Leu His Phe Ser Val
                85                  90                  95
Arg Ala Cys Ser Ser Leu Gly Val Ser Gly Gly Thr Cys Arg Glu Thr
            100                 105                 110
Phe Thr Leu Tyr Tyr Arg Gln Ala Glu Glu Pro Asp Ser Pro Asp Ser
        115                 120                 125
Val Ser Ser Trp His Leu Lys Arg Trp Thr Lys Val Asp Thr Ile Ala
    130                 135                 140
Ala Asp Glu Ser Phe Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
```

```
145                 150                 155                 160
Ser Ala Ala Trp Ala Val Gly Pro His Gly Ala Gly Gln Arg Ala Gly
                165                 170                 175
Leu Gln Leu Asn Val Lys Glu Arg Ser Phe Gly Pro Leu Thr Gln Arg
            180                 185                 190
Gly Phe Tyr Val Ala Phe Gln Asp Thr Gly Ala Cys Leu Ala Leu Val
        195                 200                 205
Ala Val Arg Leu Phe Ser Tyr Thr Cys Pro Ala Val Leu Arg Ser Phe
    210                 215                 220
Ala Ser Phe Pro Glu Thr Gln Ala Ser Gly Ala Gly Gly Ala Ser Leu
225                 230                 235                 240
Val Ala Ala Val Gly Thr Cys Val Ala His Ala Glu Pro Glu Glu Asp
                245                 250                 255
Gly Val Gly Gly Gln Ala Gly Gly Ser Pro Pro Arg Leu His Cys Asn
            260                 265                 270
Gly Glu Gly Lys Trp Met Val Ala Val Gly Gly Cys Arg Cys Gln Pro
        275                 280                 285
Gly Tyr Gln Pro Ala Arg Gly Asp Lys Ala Cys Gln Ala Cys Pro Arg
    290                 295                 300
Gly Leu Tyr Lys Ser Ser Ala Gly Asn Ala Pro Cys Ser Pro Cys Pro
305                 310                 315                 320
Ala Arg Ser His Ala Pro Asn Pro Ala Ala Pro Val Cys Pro Cys Leu
                325                 330                 335
Glu Gly Phe Tyr Arg Ala Ser Ser Asp Pro Pro Glu Ala Pro Cys Thr
            340                 345                 350
Gly Pro Pro Ser Ala Pro Gln Glu Leu Trp Phe Glu Val Gln Gly Ser
        355                 360                 365
Ala Leu Met Leu His Trp Arg Leu Pro Arg Glu Leu Gly Gly Arg Gly
    370                 375                 380
Asp Leu Leu Phe Asn Val Val Cys Lys Glu Cys Glu Gly Arg Gln Glu
385                 390                 395                 400
Pro Ala Ser Gly Gly Gly Gly Thr Cys His Arg Cys Arg Asp Glu Val
                405                 410                 415
His Phe Asp Pro Arg Gln Arg Gly Leu Thr Glu Ser Arg Val Leu Val
            420                 425                 430
Gly Gly Leu Arg Ala His Val Pro Tyr Ile Leu Glu Val Gln Ala Val
        435                 440                 445
Asn Gly Val Ser Glu Leu Ser Pro Asp Pro Pro Gln Ala Ala Ala Ile
    450                 455                 460
Asn Val Ser Thr Ser His Glu Val Pro Ser Ala Val Pro Val Val His
465                 470                 475                 480
Gln Val Ser Arg Ala Ser Asn Ser Ile Thr Val Ser Trp Pro Gln Pro
                485                 490                 495
Asp Gln Thr Asn Gly Asn Ile Leu Asp Tyr Gln Leu Arg Tyr Tyr Asp
            500                 505                 510
Gln Ala Glu Asp Glu Ser His Ser Phe Thr Leu Thr Ser Glu Thr Asn
        515                 520                 525
Thr Ala Thr Val Thr Gln Leu Ser Pro Gly His Ile Tyr Gly Phe Gln
    530                 535                 540
Val Arg Ala Arg Thr Ala Ala Gly His Gly Pro Tyr Gly Gly Lys Val
545                 550                 555                 560
Tyr Phe Gln Thr Leu Pro Gln Gly Glu Leu Ser Ser Gln Leu Pro Glu
                565                 570                 575
Arg Leu Ser Leu Val Ile Gly Ser Ile Leu Gly Ala Leu Ala Phe Leu
            580                 585                 590
Leu Leu Ala Ala Ile Thr Val Leu Ala Val Val Phe Gln Arg Lys Arg
```

595 600 605
Arg Gly Thr Gly Tyr Thr Glu Gln Leu Gln Gln Tyr Ser Ser Pro Gly
610 615 620
Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Cys
625 630 635 640
Gln Ala Ile Arg Glu Leu Ala Arg Glu Val Asp Pro Ala Tyr Ile Lys
645 650 655
Ile Glu Glu Val Ile Gly Thr Gly Ser Phe Gly Glu Val Arg Gln Gly
660 665 670
Arg Leu Gln Pro Arg Gly Arg Arg Glu Gln Thr Val Ala Ile Gln Ala
675 680 685
Leu Trp Ala Gly Gly Ala Glu Ser Leu Gln Met Thr Phe Leu Gly Arg
690 695 700
Ala Ala Val Leu Gly Gln Phe Gln His Pro Asn Ile Leu Arg Leu Glu
705 710 715 720
Gly Val Val Thr Lys Ser Arg Pro Leu Met Val Leu Thr Glu Phe Met
725 730 735
Glu Leu Gly Pro Leu Asp Ser Phe Leu Arg Gln Arg Glu Gly Gln Phe
740 745 750
Ser Ser Leu Gln Leu Val Ala Met Gln Arg Gly Val Ala Ala Ala Met
755 760 765
Gln Tyr Leu Ser Ser Phe Ala Phe Val His Arg Ser Leu Ser Ala His
770 775 780
Ser Val Leu Val Asn Ser His Leu Val Cys Lys Val Ala Arg Leu Gly
785 790 795 800
His Ser Pro Gln Gly Pro Ser Cys Leu Leu Arg Trp Ala Ala Pro Glu
805 810 815
Val Ile Ala His Gly Lys His Thr Thr Ser Ser Asp Val Trp Ser Phe
820 825 830
Gly Ile Leu Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
835 840 845
Asp Met Ser Glu Gln Glu Val Leu Asn Ala Ile Glu Gln Glu Phe Arg
850 855 860
Leu Pro Pro Pro Pro Gly Cys Pro Pro Gly Leu His Leu Leu Met Leu
865 870 875 880
Asp Thr Trp Gln Lys Asp Arg Ala Arg Arg Pro His Phe Asp Gln Leu
885 890 895
Val Ala Ala Phe Asp Lys Met Ile Arg Lys Pro Asp Thr Leu Gln Ala
900 905 910
Gly Gly Asp Pro Gly Glu Arg Pro Ser Gln Ala Leu Leu Thr Pro Val
915 920 925
Ala Leu Asp Phe Pro Cys Leu Asp Ser Pro Gln Ala Trp Leu Ser Ala
930 935 940
Ile Gly Leu Glu Cys Tyr Gln Asp Asn Phe Ser Lys Phe Gly Leu Cys
945 950 955 960
Thr Phe Ser Asp Val Ala Gln Leu Ser Leu Glu Asp Leu Pro Ala Leu
965 970 975
Gly Ile Thr Leu Ala Gly His Gln Lys Lys Leu Leu His His Ile Gln
980 985 990
Leu Leu Gln Gln His Leu Arg Gln Gln Gly Ser Val Glu Val
995 1000 1005

<210> 266
<211> 1255
<212> PRT

<213> Homo sapiens

<300>
<308> GenBank No. NP004439
<309> 2004-12-20

<400> 266

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
```

385 390 395 400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405 410 415
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420 425 430
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435 440 445
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450 455 460
Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465 470 475 480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485 490 495
Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500 505 510
Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515 520 525
Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530 535 540
Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545 550 555 560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565 570 575
Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580 585 590
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595 600 605
Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610 615 620
Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625 630 635 640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
645 650 655
Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
660 665 670
Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
675 680 685
Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
690 695 700
Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705 710 715 720
Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
725 730 735
Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
740 745 750
Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
755 760 765
Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
770 775 780
Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785 790 795 800
Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
805 810 815
Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
820 825 830
Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala

```
        835                 840                 845
Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860
Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880
Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895
Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910
Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925
Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940
Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960
Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975
Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990
Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
        995                 1000                1005
Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
    1010                1015                1020
Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025                1030                1035                1040
Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
                1045                1050                1055
Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
            1060                1065                1070
Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
        1075                1080                1085
Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
    1090                1095                1100
Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105                1110                1115                1120
Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
                1125                1130                1135
Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
            1140                1145                1150
Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
        1155                1160                1165
Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
    1170                1175                1180
Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185                1190                1195                1200
Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
                1205                1210                1215
Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
            1220                1225                1230
Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
        1235                1240                1245
Leu Gly Leu Asp Val Pro Val
    1250                1255
```

<210> 267

<211> 1342
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP001973
<309> 2004-12-20

<400> 267

```
Met Arg Ala Asn Asp Ala Leu Gln Val Leu Gly Leu Leu Phe Ser Leu
 1               5                  10                  15
Ala Arg Gly Ser Glu Val Gly Asn Ser Gln Ala Val Cys Pro Gly Thr
            20                  25                  30
Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Glu Asn Gln Tyr Gln Thr
        35                  40                  45
Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu
    50                  55                  60
Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
65                  70                  75                  80
Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr
                85                  90                  95
Leu Pro Leu Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp
            100                 105                 110
Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser
        115                 120                 125
His Ala Leu Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser
    130                 135                 140
Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
145                 150                 155                 160
Ile Asp Trp Arg Asp Ile Val Arg Asp Arg Asp Ala Glu Ile Val Val
                165                 170                 175
Lys Asp Asn Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly
            180                 185                 190
Arg Cys Trp Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr
        195                 200                 205
Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn
    210                 215                 220
Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
225                 230                 235                 240
Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
                245                 250                 255
Pro Arg Cys Pro Gln Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu
            260                 265                 270
Glu Pro Asn Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala
        275                 280                 285
Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala
    290                 295                 300
Cys Pro Pro Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys
305                 310                 315                 320
Glu Pro Cys Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser
                325                 330                 335
Gly Ser Arg Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val
            340                 345                 350
Asn Cys Thr Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu
        355                 360                 365
Asn Gly Asp Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu
```

```
    370                 375                 380
Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln
385                 390                 395                 400
Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
                405                 410                 415
Thr Ile Gly Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile
            420                 425                 430
Met Lys Asn Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu
        435                 440                 445
Ile Ser Ala Gly Arg Ile Tyr Ile Ser Ala Asn Arg Gln Leu Cys Tyr
    450                 455                 460
His His Ser Leu Asn Trp Thr Lys Val Leu Arg Gly Pro Thr Glu Glu
465                 470                 475                 480
Arg Leu Asp Ile Lys His Asn Arg Pro Arg Arg Asp Cys Val Ala Glu
                485                 490                 495
Gly Lys Val Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro
            500                 505                 510
Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Gly Gly Val
        515                 520                 525
Cys Val Thr His Cys Asn Phe Leu Asn Gly Glu Pro Arg Glu Phe Ala
    530                 535                 540
His Glu Ala Glu Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu
545                 550                 555                 560
Gly Thr Ala Thr Cys Asn Gly Ser Gly Ser Asp Thr Cys Ala Gln Cys
                565                 570                 575
Ala His Phe Arg Asp Gly Pro His Cys Val Ser Ser Cys Pro His Gly
            580                 585                 590
Val Leu Gly Ala Lys Gly Pro Ile Tyr Lys Tyr Pro Asp Val Gln Asn
        595                 600                 605
Glu Cys Arg Pro Cys His Glu Asn Cys Thr Gln Gly Cys Lys Gly Pro
    610                 615                 620
Glu Leu Gln Asp Cys Leu Gly Gln Thr Leu Val Leu Ile Gly Lys Thr
625                 630                 635                 640
His Leu Thr Met Ala Leu Thr Val Ile Ala Gly Leu Val Val Ile Phe
                645                 650                 655
Met Met Leu Gly Gly Thr Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln
            660                 665                 670
Asn Lys Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu
        675                 680                 685
Pro Leu Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe
    690                 695                 700
Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe
705                 710                 715                 720
Gly Thr Val His Lys Gly Val Trp Ile Pro Glu Gly Glu Ser Ile Lys
                725                 730                 735
Ile Pro Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser
            740                 745                 750
Phe Gln Ala Val Thr Asp His Met Leu Ala Ile Gly Ser Leu Asp His
        755                 760                 765
Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln
    770                 775                 780
Leu Val Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg
785                 790                 795                 800
Gln His Arg Gly Ala Leu Gly Pro Gln Leu Leu Leu Asn Trp Gly Val
                805                 810                 815
Gln Ile Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Gly Met Val His
```

```
            820                 825                 830
Arg Asn Leu Ala Ala Arg Asn Val Leu Leu Lys Ser Pro Ser Gln Val
        835                 840                 845
Gln Val Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys
    850                 855                 860
Gln Leu Leu Tyr Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu
865                 870                 875                 880
Glu Ser Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser
                885                 890                 895
Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr
            900                 905                 910
Ala Gly Leu Arg Leu Ala Glu Val Pro Asp Leu Leu Glu Lys Gly Glu
        915                 920                 925
Arg Leu Ala Gln Pro Gln Ile Cys Thr Ile Asp Val Tyr Met Val Met
    930                 935                 940
Val Lys Cys Trp Met Ile Asp Glu Asn Ile Arg Pro Thr Phe Lys Glu
945                 950                 955                 960
Leu Ala Asn Glu Phe Thr Arg Met Ala Arg Asp Pro Pro Arg Tyr Leu
                965                 970                 975
Val Ile Lys Arg Glu Ser Gly Pro Gly Ile Ala Pro Gly Pro Glu Pro
            980                 985                 990
His Gly Leu Thr Asn Lys Lys Leu Glu Glu Val Glu Leu Glu Pro Glu
        995                 1000                1005
Leu Asp Leu Asp Leu Asp Leu Glu Ala Glu Glu Asp Asn Leu Ala Thr
    1010                1015                1020
Thr Thr Leu Gly Ser Ala Leu Ser Leu Pro Val Gly Thr Leu Asn Arg
1025                1030                1035                1040
Pro Arg Gly Ser Gln Ser Leu Leu Ser Pro Ser Ser Gly Tyr Met Pro
                1045                1050                1055
Met Asn Gln Gly Asn Leu Gly Glu Ser Cys Gln Glu Ser Ala Val Ser
            1060                1065                1070
Gly Ser Ser Glu Arg Cys Pro Arg Pro Val Ser Leu His Pro Met Pro
        1075                1080                1085
Arg Gly Cys Leu Ala Ser Glu Ser Ser Glu Gly His Val Thr Gly Ser
    1090                1095                1100
Glu Ala Glu Leu Gln Glu Lys Val Ser Met Cys Arg Ser Arg Ser Arg
1105                1110                1115                1120
Ser Arg Ser Pro Arg Pro Arg Gly Asp Ser Ala Tyr His Ser Gln Arg
                1125                1130                1135
His Ser Leu Leu Thr Pro Val Thr Pro Leu Ser Pro Pro Gly Leu Glu
            1140                1145                1150
Glu Glu Asp Val Asn Gly Tyr Val Met Pro Asp Thr His Leu Lys Gly
        1155                1160                1165
Thr Pro Ser Ser Arg Glu Gly Thr Leu Ser Ser Val Gly Leu Ser Ser
    1170                1175                1180
Val Leu Gly Thr Glu Glu Glu Asp Glu Asp Glu Glu Tyr Glu Tyr Met
1185                1190                1195                1200
Asn Arg Arg Arg Arg His Ser Pro Pro His Pro Pro Arg Pro Ser Ser
                1205                1210                1215
Leu Glu Glu Leu Gly Tyr Glu Tyr Met Asp Val Gly Ser Asp Leu Ser
            1220                1225                1230
Ala Ser Leu Gly Ser Thr Gln Ser Cys Pro Leu His Pro Val Pro Ile
        1235                1240                1245
Met Pro Thr Ala Gly Thr Thr Pro Asp Glu Asp Tyr Glu Tyr Met Asn
    1250                1255                1260
Arg Gln Arg Asp Gly Gly Gly Pro Gly Gly Asp Tyr Ala Ala Met Gly
```

```
1265                1270                1275                1280
Ala Cys Pro Ala Ser Glu Gln Gly Tyr Glu Glu Met Arg Ala Phe Gln
                1285                1290                1295
Gly Pro Gly His Gln Ala Pro His Val His Tyr Ala Arg Leu Lys Thr
            1300                1305                1310
Leu Arg Ser Leu Glu Ala Thr Asp Ser Ala Phe Asp Asn Pro Asp Tyr
        1315                1320                1325
Trp His Ser Arg Leu Phe Pro Lys Ala Asn Ala Gln Arg Thr
    1330                1335                1340
```

<210> 268
<211> 820
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. AAA35835
<309> 2001-12-14

<400> 268

```
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
 1               5                  10                  15
Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Ala Gln
            20                  25                  30
Pro Trp Gly Ala Pro Val Glu Val Glu Ser Phe Leu Val His Pro Gly
        35                  40                  45
Asp Leu Leu Gln Leu Arg Cys Arg Leu Arg Asp Asp Val Gln Ser Ile
    50                  55                  60
Asn Trp Leu Arg Asp Gly Val Gln Leu Ala Glu Ser Asn Arg Thr Arg
65                  70                  75                  80
Ile Thr Gly Glu Glu Val Glu Val Gln Asp Ser Val Pro Ala Asp Ser
                85                  90                  95
Gly Leu Tyr Ala Cys Val Thr Ser Ser Pro Ser Gly Ser Asp Thr Thr
            100                 105                 110
Tyr Phe Ser Val Asn Val Ser Asp Ala Leu Pro Ser Ser Glu Asp Asp
        115                 120                 125
Asp Asp Asp Asp Asp Ser Ser Ser Glu Glu Lys Glu Thr Asp Asn Thr
    130                 135                 140
Lys Pro Asn Pro Val Ala Pro Tyr Trp Thr Ser Pro Glu Lys Met Glu
145                 150                 155                 160
Lys Lys Leu His Ala Val Pro Ala Ala Lys Thr Val Lys Phe Lys Cys
                165                 170                 175
Pro Ser Ser Gly Thr Pro Asn Pro Thr Leu Arg Trp Leu Lys Asn Ser
            180                 185                 190
Lys Glu Phe Lys Pro Asp His Arg Ile Gly Gly Tyr Lys Val Arg Tyr
        195                 200                 205
Ala Thr Trp Ser Ile Ile Met Asp Ser Val Val Pro Ser Asp Lys Gly
    210                 215                 220
Asn Tyr Thr Cys Ile Val Glu Asn Glu Tyr Gly Ser Ile Asn His Thr
225                 230                 235                 240
Tyr Gln Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile Leu Gln
                245                 250                 255
Ala Gly Leu Pro Ala Asn Lys Thr Val Ala Leu Gly Ser Asn Val Glu
            260                 265                 270
Phe Met Cys Lys Val Tyr Ser Asp Pro Gln Pro His Ile Gln Trp Leu
```

```
        275                 280                 285
Lys His Ile Glu Val Asn Gly Ser Lys Ile Gly Pro Asp Asn Leu Pro
    290                 295                 300
Tyr Val Gln Ile Leu Lys Thr Ala Gly Val Asn Thr Thr Asp Lys Glu
305                 310                 315                 320
Met Glu Val Leu His Leu Arg Asn Val Ser Phe Glu Asp Ala Gly Glu
                325                 330                 335
Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser His His Ser Ala
            340                 345                 350
Trp Leu Thr Val Leu Glu Ala Leu Glu Glu Arg Pro Ala Val Met Thr
        355                 360                 365
Ser Pro Leu Tyr Leu Glu Ile Ile Ile Tyr Cys Thr Gly Ala Phe Leu
    370                 375                 380
Ile Ser Cys Met Val Gly Ser Val Ile Val Tyr Lys Met Lys Ser Gly
385                 390                 395                 400
Thr Lys Lys Ser Asp Phe His Ser Gln Met Ala Val His Lys Leu Ala
                405                 410                 415
Lys Ser Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala Asp Ser Ser
            420                 425                 430
Ala Ser Met Asn Ser Gly Val Leu Leu Val Arg Pro Ser Arg Leu Ser
        435                 440                 445
Ser Ser Gly Thr Pro Met Leu Ala Gly Val Ser Glu Tyr Glu Leu Pro
    450                 455                 460
Glu Asp Pro Arg Trp Glu Leu Pro Arg Asp Arg Leu Val Leu Gly Lys
465                 470                 475                 480
Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val Leu Ala Glu Ala Ile
                485                 490                 495
Gly Leu Asp Lys Asp Lys Pro Asn Arg Val Thr Lys Val Ala Val Lys
            500                 505                 510
Met Leu Lys Ser Asp Ala Thr Glu Lys Asp Leu Ser Asp Leu Ile Ser
        515                 520                 525
Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn
    530                 535                 540
Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val Ile Val Glu
545                 550                 555                 560
Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Gln Ala Arg Arg Pro
                565                 570                 575
Pro Gly Leu Glu Tyr Cys Tyr Asn Pro Ser His Asn Pro Glu Glu Gln
            580                 585                 590
Leu Ser Ser Lys Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly
        595                 600                 605
Met Glu Tyr Leu Ala Ser Lys Lys Cys Ile His Arg Asp Leu Ala Ala
    610                 615                 620
Arg Asn Val Leu Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe
625                 630                 635                 640
Gly Leu Ala Arg Asp Ile His His Ile Asp Tyr Tyr Lys Lys Thr Thr
                645                 650                 655
Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp
            660                 665                 670
Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
        675                 680                 685
Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly Val Pro Val
    690                 695                 700
Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro
705                 710                 715                 720
Ser Asn Cys Thr Asn Glu Leu Tyr Met Met Met Arg Asp Cys Trp His
```

```
                725                 730                 735
Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu
            740                 745                 750
Asp Arg Ile Val Ala Leu Thr Ser Asn Gln Glu Tyr Leu Asp Leu Ser
        755                 760                 765
Met Pro Leu Asp Gln Tyr Ser Pro Ser Phe Pro Asp Thr Arg Ser Ser
    770                 775                 780
Thr Cys Ser Ser Gly Glu Asp Ser Val Phe Ser His Glu Pro Leu Pro
785                 790                 795                 800
Glu Glu Pro Cys Leu Pro Arg His Pro Ala Gln Leu Ala Asn Gly Gly
                805                 810                 815
Leu Lys Arg Arg
            820
```

<210> 269
<211> 821
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP000132
<309> 2004-12-20

```
<400> 269
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
 1               5                  10                  15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
            20                  25                  30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
        35                  40                  45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
    50                  55                  60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65                  70                  75                  80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
                85                  90                  95
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
            100                 105                 110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
        115                 120                 125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
    130                 135                 140
Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145                 150                 155                 160
Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
                165                 170                 175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
            180                 185                 190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
        195                 200                 205
Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
    210                 215                 220
Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225                 230                 235                 240
Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
```

```
                245                 250                 255
Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
            260                 265                 270
Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
        275                 280                 285
Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
    290                 295                 300
Gly Leu Pro Tyr Leu Lys Val Leu Lys Ala Ala Gly Val Asn Thr Thr
305                 310                 315                 320
Asp Lys Glu Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe Glu Asp
                325                 330                 335
Ala Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Ile Ser Phe
            340                 345                 350
His Ser Ala Trp Leu Thr Val Leu Pro Ala Pro Gly Arg Glu Lys Glu
        355                 360                 365
Ile Thr Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile Gly
    370                 375                 380
Val Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg Met
385                 390                 395                 400
Lys Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val His
                405                 410                 415
Lys Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala
            420                 425                 430
Glu Ser Ser Ser Ser Met Asn Ser Asn Thr Pro Leu Val Arg Ile Thr
        435                 440                 445
Thr Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val Ser
    450                 455                 460
Glu Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp Lys
465                 470                 475                 480
Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val
                485                 490                 495
Met Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala Val
            500                 505                 510
Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp Leu
        515                 520                 525
Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His
    530                 535                 540
Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu
545                 550                 555                 560
Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu
                565                 570                 575
Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg
            580                 585                 590
Val Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr
        595                 600                 605
Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His
    610                 615                 620
Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met
625                 630                 635                 640
Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr
                645                 650                 655
Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro
            660                 665                 670
Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser
        675                 680                 685
Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr
```

```
    690                 695                 700
Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His
705                 710                 715                 720
Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met Met
                725                 730                 735
Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln
            740                 745                 750
Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu Glu
        755                 760                 765
Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr Pro
    770                 775                 780
Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser Pro
785                 790                 795                 800
Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile Asn
                805                 810                 815
Gly Ser Val Lys Thr
            820


<210> 270
<211> 806
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP000133
<309> 2004-12-20

<400> 270
Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile
 1               5                  10                  15
Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val
            20                  25                  30
Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln
        35                  40                  45
Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro
    50                  55                  60
Gly Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly
65                  70                  75                  80
Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val
                85                  90                  95
Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg
            100                 105                 110
Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala
        115                 120                 125
Pro Ser Ser Gly Asp Asp Glu Asp Gly Glu Asp Glu Ala Glu Asp Thr
    130                 135                 140
Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp
145                 150                 155                 160
Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys
                165                 170                 175
Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly
            180                 185                 190
Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His
        195                 200                 205
Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly
```

```
    210                 215                 220
Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr
225                 230                 235                 240
Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln
                245                 250                 255
Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu
            260                 265                 270
Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu
        275                 280                 285
Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro
    290                 295                 300
Tyr Val Thr Val Leu Lys Thr Ala Gly Ala Asn Thr Thr Asp Lys Glu
305                 310                 315                 320
Leu Glu Val Leu Ser Leu His Asn Val Thr Phe Glu Asp Ala Gly Glu
                325                 330                 335
Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Phe Ser His His Ser Ala
            340                 345                 350
Trp Leu Val Val Leu Pro Ala Glu Glu Glu Leu Val Glu Ala Asp Glu
        355                 360                 365
Ala Gly Ser Val Tyr Ala Gly Ile Leu Ser Tyr Gly Val Gly Phe Phe
    370                 375                 380
Leu Phe Ile Leu Val Val Ala Ala Val Thr Leu Cys Arg Leu Arg Ser
385                 390                 395                 400
Pro Pro Lys Lys Gly Leu Gly Ser Pro Thr Val His Lys Ile Ser Arg
                405                 410                 415
Phe Pro Leu Lys Arg Gln Val Ser Leu Glu Ser Asn Ala Ser Met Ser
            420                 425                 430
Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly
        435                 440                 445
Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys
    450                 455                 460
Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu
465                 470                 475                 480
Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys
                485                 490                 495
Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp
            500                 505                 510
Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met
        515                 520                 525
Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala
    530                 535                 540
Cys Thr Gln Gly Gly Pro Leu Tyr Val Leu Val Glu Tyr Ala Ala Lys
545                 550                 555                 560
Gly Asn Leu Arg Glu Phe Leu Arg Ala Arg Arg Pro Pro Gly Leu Asp
                565                 570                 575
Tyr Ser Phe Asp Thr Cys Lys Pro Pro Glu Glu Gln Leu Thr Phe Lys
            580                 585                 590
Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu
        595                 600                 605
Ala Ser Gln Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu
    610                 615                 620
Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg
625                 630                 635                 640
Asp Val His Asn Leu Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu
                645                 650                 655
Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr
```

```
            660                 665                 670
His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe
        675                 680                 685
Thr Leu Gly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe
    690                 695                 700
Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn Cys Thr
705                 710                 715                 720
His Asp Leu Tyr Met Ile Met Arg Glu Cys Trp His Ala Ala Pro Ser
                725                 730                 735
Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Val Leu
            740                 745                 750
Thr Val Thr Ser Thr Asp Glu Tyr Leu Asp Leu Ser Ala Pro Phe Glu
        755                 760                 765
Gln Tyr Ser Pro Gly Gly Gln Asp Thr Pro Ser Ser Ser Ser Ser Gly
    770                 775                 780
Asp Asp Ser Val Phe Ala His Asp Leu Leu Pro Pro Ala Pro Pro Ser
785                 790                 795                 800
Ser Gly Gly Ser Arg Thr
                805
```

<210> 271
<211> 802
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002002
<309> 2004-10-28

<400> 271

```
Met Arg Leu Leu Leu Ala Leu Leu Gly Val Leu Leu Ser Val Pro Gly
 1               5                  10                  15
Pro Pro Val Leu Ser Leu Glu Ala Ser Glu Glu Val Glu Leu Glu Pro
            20                  25                  30
Cys Leu Ala Pro Ser Leu Glu Gln Gln Glu Gln Glu Leu Thr Val Ala
        35                  40                  45
Leu Gly Gln Pro Val Arg Leu Cys Cys Gly Arg Ala Glu Arg Gly Gly
    50                  55                  60
His Trp Tyr Lys Glu Gly Ser Arg Leu Ala Pro Ala Gly Arg Val Arg
65                  70                  75                  80
Gly Trp Arg Gly Arg Leu Glu Ile Ala Ser Phe Leu Pro Glu Asp Ala
                85                  90                  95
Gly Arg Tyr Leu Cys Leu Ala Arg Gly Ser Met Ile Val Leu Gln Asn
            100                 105                 110
Leu Thr Leu Ile Thr Gly Asp Ser Leu Thr Ser Ser Asn Asp Asp Glu
        115                 120                 125
Asp Pro Lys Ser His Arg Asp Pro Ser Asn Arg His Ser Tyr Pro Gln
    130                 135                 140
Gln Ala Pro Tyr Trp Thr His Pro Gln Arg Met Glu Lys Lys Leu His
145                 150                 155                 160
Ala Val Pro Ala Gly Asn Thr Val Lys Phe Arg Cys Pro Ala Ala Gly
                165                 170                 175
Asn Pro Thr Pro Thr Ile Arg Trp Leu Lys Asp Gly Gln Ala Phe His
            180                 185                 190
Gly Glu Asn Arg Ile Gly Gly Ile Arg Leu Arg His Gln His Trp Ser
```

```
        195                 200                 205
Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly Thr Tyr Thr Cys
    210                 215                 220
Leu Val Glu Asn Ala Val Gly Ser Ile Arg Tyr Asn Tyr Leu Leu Asp
225                 230                 235                 240
Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro
                245                 250                 255
Ala Asn Thr Thr Ala Val Val Gly Ser Asp Val Glu Leu Leu Cys Lys
            260                 265                 270
Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu Lys His Ile Val
        275                 280                 285
Ile Asn Gly Ser Ser Phe Gly Ala Asp Gly Phe Pro Tyr Val Gln Val
    290                 295                 300
Leu Lys Thr Ala Asp Ile Asn Ser Ser Glu Val Glu Val Leu Tyr Leu
305                 310                 315                 320
Arg Asn Val Ser Ala Glu Asp Ala Gly Glu Tyr Thr Cys Leu Ala Gly
                325                 330                 335
Asn Ser Ile Gly Leu Ser Tyr Gln Ser Ala Trp Leu Thr Val Leu Pro
            340                 345                 350
Glu Glu Asp Pro Thr Trp Thr Ala Ala Ala Pro Glu Ala Arg Tyr Thr
        355                 360                 365
Asp Ile Ile Leu Tyr Ala Ser Gly Ser Leu Ala Leu Ala Val Leu Leu
    370                 375                 380
Leu Leu Ala Gly Leu Tyr Arg Gly Gln Ala Leu His Gly Arg His Pro
385                 390                 395                 400
Arg Pro Pro Ala Thr Val Gln Lys Leu Ser Arg Phe Pro Leu Ala Arg
                405                 410                 415
Gln Phe Ser Leu Glu Ser Gly Ser Ser Gly Lys Ser Ser Ser Ser Leu
            420                 425                 430
Val Arg Gly Val Arg Leu Ser Ser Ser Gly Pro Ala Leu Leu Ala Gly
        435                 440                 445
Leu Val Ser Leu Asp Leu Pro Leu Asp Pro Leu Trp Glu Phe Pro Arg
    450                 455                 460
Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln
465                 470                 475                 480
Val Val Arg Ala Glu Ala Phe Gly Met Asp Pro Ala Arg Pro Asp Gln
                485                 490                 495
Ala Ser Thr Val Ala Val Lys Met Leu Lys Asp Asn Ala Ser Asp Lys
            500                 505                 510
Asp Leu Ala Asp Leu Val Ser Glu Met Glu Val Met Lys Leu Ile Gly
        515                 520                 525
Arg His Lys Asn Ile Ile Asn Leu Leu Gly Val Cys Thr Gln Glu Gly
    530                 535                 540
Pro Leu Tyr Val Ile Val Glu Cys Ala Ala Lys Gly Asn Leu Arg Glu
545                 550                 555                 560
Phe Leu Arg Ala Arg Arg Pro Pro Gly Pro Asp Leu Ser Pro Asp Gly
                565                 570                 575
Pro Arg Ser Ser Glu Gly Pro Leu Ser Phe Pro Val Leu Val Ser Cys
            580                 585                 590
Ala Tyr Gln Val Ala Arg Gly Met Gln Tyr Leu Glu Ser Arg Lys Cys
        595                 600                 605
Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asp Asn
    610                 615                 620
Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Gly Val His His Ile
625                 630                 635                 640
Asp Tyr Tyr Lys Lys Thr Ser Asn Gly Arg Leu Pro Val Lys Trp Met
```

```
                645                 650                 655
Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val
            660                 665                 670
Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly Ser
        675                 680                 685
Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Ser Leu Leu Arg Glu
    690                 695                 700
Gly His Arg Met Asp Arg Pro Pro His Cys Pro Pro Glu Leu Tyr Gly
705                 710                 715                 720
Leu Met Arg Glu Cys Trp His Ala Ala Pro Ser Gln Arg Pro Thr Phe
                725                 730                 735
Lys Gln Leu Val Glu Ala Leu Asp Lys Val Leu Leu Ala Val Ser Glu
            740                 745                 750
Glu Tyr Leu Asp Leu Arg Leu Thr Phe Gly Pro Tyr Ser Pro Ser Gly
        755                 760                 765
Gly Asp Ala Ser Ser Thr Cys Ser Ser Ser Asp Ser Val Phe Ser His
    770                 775                 780
Asp Pro Leu Pro Leu Gly Ser Ser Ser Phe Pro Phe Gly Ser Gly Val
785                 790                 795                 800
Gln Thr
```

<210> 272
<211> 993
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP004110
<309> 2005-01-22

<400> 272

```
Met Pro Ala Leu Ala Arg Asp Ala Gly Thr Val Pro Leu Leu Val Val
 1               5                  10                  15
Phe Ser Ala Met Ile Phe Gly Thr Ile Thr Asn Gln Asp Leu Pro Val
            20                  25                  30
Ile Lys Cys Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly
        35                  40                  45
Lys Ser Ser Ser Tyr Pro Met Val Ser Glu Ser Pro Glu Asp Leu Gly
    50                  55                  60
Cys Ala Leu Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Ala
65                  70                  75                  80
Val Glu Val Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp
                85                  90                  95
Ala Pro Gly Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu
            100                 105                 110
Asn Cys Gln Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met
        115                 120                 125
Val Ile Leu Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe
    130                 135                 140
Ile Gln Ser Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile
145                 150                 155                 160
Arg Asn Thr Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met
                165                 170                 175
Glu Asn Gln Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro
```

```
            180                 185                 190
Ile Val Glu Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu
        195                 200                 205
Glu Ser Pro Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu
    210                 215                 220
Phe Gly Thr Asp Ile Arg Cys Cys Ala Arg Asn Glu Leu Gly Arg Glu
225                 230                 235                 240
Cys Thr Arg Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr
                245                 250                 255
Leu Pro Gln Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys
            260                 265                 270
Lys Ala Val His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu
        275                 280                 285
Asn Lys Ala Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser
    290                 295                 300
Thr Asn Arg Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val
305                 310                 315                 320
Ala Arg Asn Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro
                325                 330                 335
Ser Gln Ser Ala Leu Val Thr Ile Val Gly Lys Gly Phe Ile Asn Ala
            340                 345                 350
Thr Asn Ser Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys
        355                 360                 365
Phe Ser Val Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr
    370                 375                 380
Phe Ser Arg Lys Ser Phe Pro Cys Glu Gln Lys Gly Leu Asp Asn Gly
385                 390                 395                 400
Tyr Ser Ile Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr
                405                 410                 415
Ile Phe His Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr
            420                 425                 430
Leu Asn Ile Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser
        435                 440                 445
Gln Ala Ser Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp
    450                 455                 460
Lys Lys Cys Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu
465                 470                 475                 480
Gly Val Trp Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val
                485                 490                 495
Ser Ser Ser Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val
            500                 505                 510
Lys Cys Cys Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu
        515                 520                 525
Leu Asn Ser Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Ile Ser Phe
    530                 535                 540
Tyr Ala Thr Ile Gly Val Cys Leu Leu Phe Ile Val Val Leu Thr Leu
545                 550                 555                 560
Leu Ile Cys His Lys Tyr Lys Lys Gln Phe Arg Tyr Glu Ser Gln Leu
                565                 570                 575
Gln Met Val Gln Val Thr Gly Ser Ser Asp Asn Glu Tyr Phe Tyr Val
            580                 585                 590
Asp Phe Arg Glu Tyr Glu Tyr Asp Leu Lys Trp Glu Phe Pro Arg Glu
        595                 600                 605
Asn Leu Glu Phe Gly Lys Val Leu Gly Ser Gly Ala Phe Gly Lys Val
    610                 615                 620
Met Asn Ala Thr Ala Tyr Gly Ile Ser Lys Thr Gly Val Ser Ile Gln
```

625 630 635 640
Val Ala Val Lys Met Leu Lys Glu Lys Ala Asp Ser Ser Glu Arg Glu
645 650 655
Ala Leu Met Ser Glu Leu Lys Met Met Thr Gln Leu Gly Ser His Glu
660 665 670
Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Leu Ser Gly Pro Ile Tyr
675 680 685
Leu Ile Phe Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Tyr Leu Arg
690 695 700
Ser Lys Arg Glu Lys Phe His Arg Thr Trp Thr Glu Ile Phe Lys Glu
705 710 715 720
His Asn Phe Ser Phe Tyr Pro Thr Phe Gln Ser His Pro Asn Ser Ser
725 730 735
Met Pro Gly Ser Arg Glu Val Gln Ile His Pro Asp Ser Asp Gln Ile
740 745 750
Ser Gly Leu His Gly Asn Ser Phe His Ser Glu Asp Glu Ile Glu Tyr
755 760 765
Glu Asn Gln Lys Arg Leu Glu Glu Glu Glu Asp Leu Asn Val Leu Thr
770 775 780
Phe Glu Asp Leu Leu Cys Phe Ala Tyr Gln Val Ala Lys Gly Met Glu
785 790 795 800
Phe Leu Glu Phe Lys Ser Cys Val His Arg Asp Leu Ala Ala Arg Asn
805 810 815
Val Leu Val Thr His Gly Lys Val Val Lys Ile Cys Asp Phe Gly Leu
820 825 830
Ala Arg Asp Ile Met Ser Asp Ser Asn Tyr Val Val Arg Gly Asn Ala
835 840 845
Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Leu Phe Glu Gly Ile
850 855 860
Tyr Thr Ile Lys Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu
865 870 875 880
Ile Phe Ser Leu Gly Val Asn Pro Tyr Pro Gly Ile Pro Val Asp Ala
885 890 895
Asn Phe Tyr Lys Leu Ile Gln Asn Gly Phe Lys Met Asp Gln Pro Phe
900 905 910
Tyr Ala Thr Glu Glu Ile Tyr Ile Ile Met Gln Ser Cys Trp Ala Phe
915 920 925
Asp Ser Arg Lys Arg Pro Ser Phe Pro Asn Leu Thr Ser Phe Leu Gly
930 935 940
Cys Gln Leu Ala Asp Ala Glu Glu Ala Met Tyr Gln Asn Val Asp Gly
945 950 955 960
Arg Val Ser Glu Cys Pro His Thr Tyr Gln Asn Arg Arg Pro Phe Ser
965 970 975
Arg Glu Met Asp Leu Gly Leu Leu Ser Pro Gln Ala Gln Val Glu Asp
980 985 990
Ser

<210> 273
<211> 1363
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP000213

<309> 2004-12-20

<400> 273

```
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
 1               5                  10                  15
Leu Leu Asp Gly Leu Val Ser Asp Tyr Ser Met Thr Pro Pro Thr Leu
            20                  25                  30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
        35                  40                  45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
    50                  55                  60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65                  70                  75                  80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
                85                  90                  95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
            100                 105                 110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
        115                 120                 125
Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
    130                 135                 140
Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145                 150                 155                 160
Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
                165                 170                 175
Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
            180                 185                 190
Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
        195                 200                 205
Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
    210                 215                 220
Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225                 230                 235                 240
Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
                245                 250                 255
Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
            260                 265                 270
Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
        275                 280                 285
Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
    290                 295                 300
Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305                 310                 315                 320
Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
                325                 330                 335
Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
            340                 345                 350
Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
        355                 360                 365
Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
    370                 375                 380
Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385                 390                 395                 400
Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
                405                 410                 415
Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
```

```
                420                 425                 430
Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
        435                 440                 445
Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr
    450                 455                 460
Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465                 470                 475                 480
Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp
                485                 490                 495
Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
            500                 505                 510
Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
        515                 520                 525
Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
    530                 535                 540
Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile
545                 550                 555                 560
Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
                565                 570                 575
Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
            580                 585                 590
Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
        595                 600                 605
Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
    610                 615                 620
Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
625                 630                 635                 640
Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
                645                 650                 655
Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
            660                 665                 670
Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
        675                 680                 685
Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
    690                 695                 700
His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705                 710                 715                 720
Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
                725                 730                 735
Arg Val Arg Glu Glu Asp Ala Gly Pro Tyr Leu Cys Ser Val Cys Arg
            740                 745                 750
Pro Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser
        755                 760                 765
Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val
    770                 775                 780
Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met
785                 790                 795                 800
Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile
                805                 810                 815
Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser
            820                 825                 830
Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
        835                 840                 845
Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala
    850                 855                 860
Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met
```

865 870 875 880
Leu Lys Glu Gly Ala Thr Ala Ser Glu Gln Arg Ala Leu Met Ser Glu
885 890 895
Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu
900 905 910
Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu
915 920 925
Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp
930 935 940
Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe
945 950 955 960
Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser
965 970 975
Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala
980 985 990
Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro
995 1000 1005
Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg Gly
1010 1015 1020
Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala
1025 1030 1035 1040
Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile Cys Asp Phe
1045 1050 1055
Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
1060 1065 1070
Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asp
1075 1080 1085
Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
1090 1095 1100
Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile
1105 1110 1115 1120
Asn Glu Glu Phe Cys Gln Arg Val Arg Asp Gly Thr Arg Met Arg Ala
1125 1130 1135
Pro Glu Leu Ala Thr Pro Ala Ile Arg His Ile Met Leu Asn Cys Trp
1140 1145 1150
Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Glu Leu Val Glu Ile
1155 1160 1165
Leu Gly Asp Leu Leu Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val
1170 1175 1180
Cys Met Ala Pro Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser
1185 1190 1195 1200
Gln Val Ser Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp
1205 1210 1215
Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn
1220 1225 1230
Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
1235 1240 1245
Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr Thr
1250 1255 1260
Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala
1265 1270 1275 1280
Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln Glu Ser Gly
1285 1290 1295
Phe Ser Cys Lys Gly Pro Gly Gln Asn Val Ala Val Thr Arg Ala His
1300 1305 1310
Pro Asp Ser Gln Gly Arg Arg Arg Arg Pro Glu Arg Gly Ala Arg Gly

```
        1315                1320                1325
Gly Gln Val Phe Tyr Asn Ser Glu Tyr Gly Glu Leu Ser Glu Pro Ser
    1330                1335                1340
Glu Glu Asp His Cys Ser Pro Ser Ala Arg Val Thr Phe Phe Thr Asp
1345                1350                1355                1360
Asn Ser Tyr
```

<210> 274
<211> 1390
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP000236
<309> 2004-10-28

<400> 274

```
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1               5                  10                  15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30
Ser Glu Met Asn Val Asn Met Lys Tyr Gln Leu Pro Asn Phe Thr Ala
        35                  40                  45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110
Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
```

```
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480
Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
```

```
            740                 745                 750
Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780
Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800
Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815
Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830
Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845
Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
    850                 855                 860
Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865                 870                 875                 880
Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
                885                 890                 895
Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys
            900                 905                 910
Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp
        915                 920                 925
Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
    930                 935                 940
Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln
945                 950                 955                 960
Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His
                965                 970                 975
Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
            980                 985                 990
Thr Glu Met Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro
        995                 1000                1005
Glu Asp Gln Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln Val
    1010                1015                1020
Gln Tyr Pro Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly Asp Ser
1025                1030                1035                1040
Asp Ile Ser Ser Pro Leu Leu Gln Asn Thr Val His Ile Asp Leu Ser
                1045                1050                1055
Ala Leu Asn Pro Glu Leu Val Gln Ala Val Gln His Val Val Ile Gly
            1060                1065                1070
Pro Ser Ser Leu Ile Val His Phe Asn Glu Val Ile Gly Arg Gly His
        1075                1080                1085
Phe Gly Cys Val Tyr His Gly Thr Leu Leu Asp Asn Asp Gly Lys Lys
    1090                1095                1100
Ile His Cys Ala Val Lys Ser Leu Asn Arg Ile Thr Asp Ile Gly Glu
1105                1110                1115                1120
Val Ser Gln Phe Leu Thr Glu Gly Ile Ile Met Lys Asp Phe Ser His
                1125                1130                1135
Pro Asn Val Leu Ser Leu Leu Gly Ile Cys Leu Arg Ser Glu Gly Ser
            1140                1145                1150
Pro Leu Val Val Leu Pro Tyr Met Lys His Gly Asp Leu Arg Asn Phe
        1155                1160                1165
Ile Arg Asn Glu Thr His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe
    1170                1175                1180
Gly Leu Gln Val Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe
```

```
1185                1190                1195                1200
Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe
                1205                1210                1215
Thr Val Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys
            1220                1225                1230
Glu Tyr Tyr Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys
        1235                1240                1245
Trp Met Ala Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys Ser
    1250                1255                1260
Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Leu Met Thr Arg Gly
1265                1270                1275                1280
Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr Val Tyr Leu
                1285                1290                1295
Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu Tyr Cys Pro Asp Pro Leu
            1300                1305                1310
Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg Pro
        1315                1320                1325
Ser Phe Ser Glu Leu Val Ser Arg Ile Ser Ala Ile Phe Ser Thr Phe
    1330                1335                1340
Ile Gly Glu His Tyr Val His Val Asn Ala Thr Tyr Val Asn Val Lys
1345                1350                1355                1360
Cys Val Ala Pro Tyr Pro Ser Leu Leu Ser Ser Glu Asp Asn Ala Asp
                1365                1370                1375
Asp Glu Val Asp Thr Arg Pro Ala Ser Phe Trp Glu Thr Ser
            1380                1385                1390


<210> 275
<211> 1089
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP006197
<309> 2004-10-26

<400> 275
Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
 1               5                  10                  15
Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
            20                  25                  30
Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
        35                  40                  45
Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
    50                  55                  60
Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65                  70                  75                  80
Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
                85                  90                  95
Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
            100                 105                 110
Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
        115                 120                 125
Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
    130                 135                 140
Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
```

```
145                 150                 155                 160
Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
                165                 170                 175
Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
            180                 185                 190
Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
        195                 200                 205
Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
    210                 215                 220
Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225                 230                 235                 240
Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
                245                 250                 255
Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
            260                 265                 270
Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
        275                 280                 285
Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
    290                 295                 300
Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
305                 310                 315                 320
Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
                325                 330                 335
Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
            340                 345                 350
Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
        355                 360                 365
Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
    370                 375                 380
Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
385                 390                 395                 400
Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
                405                 410                 415
Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
            420                 425                 430
Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
        435                 440                 445
Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
    450                 455                 460
Leu Ala Asn Asn Val Ser Asn Ile Ile Thr Glu Ile His Ser Arg Asp
465                 470                 475                 480
Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
                485                 490                 495
Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
            500                 505                 510
Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
        515                 520                 525
Ala Ala Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val
    530                 535                 540
Leu Val Val Ile Trp Lys Gln Lys Pro Arg Tyr Glu Ile Arg Trp Arg
545                 550                 555                 560
Val Ile Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp
                565                 570                 575
Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly
            580                 585                 590
Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val
```

595 600 605
Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
610 615 620
Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
625 630 635 640
Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
645 650 655
Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
660 665 670
Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys
675 680 685
Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
690 695 700
Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
705 710 715 720
Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
725 730 735
Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
740 745 750
Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
755 760 765
Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
770 775 780
Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
785 790 795 800
Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
805 810 815
Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
820 825 830
Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
835 840 845
Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
850 855 860
Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
865 870 875 880
Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
885 890 895
Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
900 905 910
Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
915 920 925
Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
930 935 940
His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
945 950 955 960
Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
965 970 975
Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
980 985 990
Tyr Lys Asn Glu Glu Asp Lys Leu Lys Asp Trp Glu Gly Gly Leu Asp
995 1000 1005
Glu Gln Arg Leu Ser Ala Asp Ser Gly Tyr Ile Ile Pro Leu Pro Asp
1010 1015 1020
Ile Asp Pro Val Pro Glu Glu Glu Asp Leu Gly Lys Arg Asn Arg His
1025 1030 1035 1040
Ser Ser Gln Thr Ser Glu Glu Ser Ala Ile Glu Thr Gly Ser Ser Ser

```
                1045                1050                1055
Ser Thr Phe Ile Lys Arg Glu Asp Glu Thr Ile Glu Asp Ile Asp Met
            1060                1065                1070
Met Asp Asp Ile Gly Ile Asp Ser Ser Asp Leu Val Glu Asp Ser Phe
        1075                1080                1085
Leu
```

<210> 276
<211> 1106
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002600
<309> 2004-10-26

<400> 276

```
Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
 1               5                  10                  15
Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser Gln Gly
            20                  25                  30
Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
        35                  40                  45
Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
    50                  55                  60
Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65                  70                  75                  80
Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
                85                  90                  95
Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
            100                 105                 110
Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly Phe Leu
        115                 120                 125
Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
    130                 135                 140
Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145                 150                 155                 160
His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
                165                 170                 175
Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
            180                 185                 190
Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg
        195                 200                 205
Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
    210                 215                 220
Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225                 230                 235                 240
Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
                245                 250                 255
Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
            260                 265                 270
Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
        275                 280                 285
Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
```

```
    290                 295                 300
Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu Leu Gly
305                 310                 315                 320
Glu Val Gly Thr Leu Gln Phe Ala Glu Leu His Arg Ser Arg Thr Leu
                325                 330                 335
Gln Val Val Phe Glu Ala Tyr Pro Pro Pro Thr Val Leu Trp Phe Lys
            340                 345                 350
Asp Asn Arg Thr Leu Gly Asp Ser Ser Ala Gly Glu Ile Ala Leu Ser
        355                 360                 365
Thr Arg Asn Val Ser Glu Thr Arg Tyr Val Ser Glu Leu Thr Leu Val
    370                 375                 380
Arg Val Lys Val Ala Glu Ala Gly His Tyr Thr Met Arg Ala Phe His
385                 390                 395                 400
Glu Asp Ala Glu Val Gln Leu Ser Phe Gln Leu Gln Ile Asn Val Pro
                405                 410                 415
Val Arg Val Leu Glu Leu Ser Glu Ser His Pro Asp Ser Gly Glu Gln
            420                 425                 430
Thr Val Arg Cys Arg Gly Arg Gly Met Pro Gln Pro Asn Ile Ile Trp
        435                 440                 445
Ser Ala Cys Arg Asp Leu Lys Arg Cys Pro Arg Glu Leu Pro Pro Thr
    450                 455                 460
Leu Leu Gly Asn Ser Ser Glu Glu Glu Ser Gln Leu Glu Thr Asn Val
465                 470                 475                 480
Thr Tyr Trp Glu Glu Glu Gln Glu Phe Glu Val Val Ser Thr Leu Arg
                485                 490                 495
Leu Gln His Val Asp Arg Pro Leu Ser Val Arg Cys Thr Leu Arg Asn
            500                 505                 510
Ala Val Gly Gln Asp Thr Gln Glu Val Ile Val Val Pro His Ser Leu
        515                 520                 525
Pro Phe Lys Val Val Val Ile Ser Ala Ile Leu Ala Leu Val Val Leu
    530                 535                 540
Thr Ile Ile Ser Leu Ile Ile Leu Ile Met Leu Trp Gln Lys Lys Pro
545                 550                 555                 560
Arg Tyr Glu Ile Arg Trp Lys Val Ile Glu Ser Val Ser Ser Asp Gly
                565                 570                 575
His Glu Tyr Ile Tyr Val Asp Pro Met Gln Leu Pro Tyr Asp Ser Thr
            580                 585                 590
Trp Glu Leu Pro Arg Asp Gln Leu Val Leu Gly Arg Thr Leu Gly Ser
        595                 600                 605
Gly Ala Phe Gly Gln Val Val Glu Ala Thr Ala His Gly Leu Ser His
    610                 615                 620
Ser Gln Ala Thr Met Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala
625                 630                 635                 640
Arg Ser Ser Glu Lys Gln Ala Leu Met Ser Glu Leu Lys Ile Met Ser
                645                 650                 655
His Leu Gly Pro His Leu Asn Val Val Asn Leu Leu Gly Ala Cys Thr
            660                 665                 670
Lys Gly Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Arg Tyr Gly Asp
        675                 680                 685
Leu Val Asp Tyr Leu His Arg Asn Lys His Thr Phe Leu Gln His His
    690                 695                 700
Ser Asp Lys Arg Arg Pro Pro Ser Ala Glu Leu Tyr Ser Asn Ala Leu
705                 710                 715                 720
Pro Val Gly Leu Pro Leu Pro Ser His Val Ser Leu Thr Gly Glu Ser
                725                 730                 735
Asp Gly Gly Tyr Met Asp Met Ser Lys Asp Glu Ser Val Asp Tyr Val
```

```
            740                 745                 750
Pro Met Leu Asp Met Lys Gly Asp Val Lys Tyr Ala Asp Ile Glu Ser
        755                 760                 765
Ser Asn Tyr Met Ala Pro Tyr Asp Asn Tyr Val Pro Ser Ala Pro Glu
    770                 775                 780
Arg Thr Cys Arg Ala Thr Leu Ile Asn Glu Ser Pro Val Leu Ser Tyr
785                 790                 795                 800
Met Asp Leu Val Gly Phe Ser Tyr Gln Val Ala Asn Gly Met Glu Phe
                805                 810                 815
Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn Val
            820                 825                 830
Leu Ile Cys Glu Gly Lys Leu Val Lys Ile Cys Asp Phe Gly Leu Ala
        835                 840                 845
Arg Asp Ile Met Arg Asp Ser Asn Tyr Ile Ser Lys Gly Ser Thr Phe
    850                 855                 860
Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Ser Leu Tyr
865                 870                 875                 880
Thr Thr Leu Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile
                885                 890                 895
Phe Thr Leu Gly Gly Thr Pro Tyr Pro Glu Leu Pro Met Asn Glu Gln
            900                 905                 910
Phe Tyr Asn Ala Ile Lys Arg Gly Tyr Arg Met Ala Gln Pro Ala His
        915                 920                 925
Ala Ser Asp Glu Ile Tyr Glu Ile Met Gln Lys Cys Trp Glu Glu Lys
    930                 935                 940
Phe Glu Ile Arg Pro Pro Phe Ser Gln Leu Val Leu Leu Leu Glu Arg
945                 950                 955                 960
Leu Leu Gly Glu Gly Tyr Lys Lys Lys Tyr Gln Gln Val Asp Glu Glu
                965                 970                 975
Phe Leu Arg Ser Asp His Pro Ala Ile Leu Arg Ser Gln Ala Arg Leu
            980                 985                 990
Pro Gly Phe His Gly Leu Arg Ser Pro Leu Asp Thr Ser Ser Val Leu
        995                 1000                1005
Tyr Thr Ala Val Gln Pro Asn Glu Gly Asp Asn Asp Tyr Ile Ile Pro
    1010                1015                1020
Leu Pro Asp Pro Lys Pro Glu Val Ala Asp Glu Gly Pro Leu Glu Gly
1025                1030                1035                1040
Ser Pro Ser Leu Ala Ser Ser Thr Leu Asn Glu Val Asn Thr Ser Ser
                1045                1050                1055
Thr Ile Ser Cys Asp Ser Pro Leu Glu Pro Gln Asp Glu Pro Glu Pro
            1060                1065                1070
Glu Pro Gln Leu Glu Leu Gln Val Glu Pro Glu Pro Glu Leu Glu Gln
        1075                1080                1085
Leu Pro Asp Ser Gly Cys Pro Ala Pro Arg Ala Glu Ala Glu Asp Ser
    1090                1095                1100
Phe Leu
1105
```

<210> 277
<211> 1400
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002438

<309> 2004-10-28

<400> 277

```
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1               5                  10                  15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20                  25                  30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35                  40                  45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50                  55                  60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65                  70                  75                  80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85                  90                  95
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100                 105                 110
Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115                 120                 125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145                 150                 155                 160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205
Gly Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Gln Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415
Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
```

```
            420                 425                 430
Phe Ser Arg Val Asp Leu Phe Asn Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445
Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460
Gly Thr Met Asp Gly Arg Ile Leu Gln Val Glu Leu Val Arg Ser Leu
465                 470                 475                 480
Asn Tyr Leu Leu Tyr Val Ser Asn Phe Ser Leu Gly Asp Ser Gly Gln
                485                 490                 495
Pro Val Gln Arg Asp Val Ser Arg Leu Gly Asp His Leu Leu Phe Ala
            500                 505                 510
Ser Gly Asp Gln Val Phe Gln Val Pro Ile Arg Gly Pro Gly Cys Arg
        515                 520                 525
His Phe Leu Thr Cys Gly Arg Cys Leu Arg Ala Trp His Phe Met Gly
    530                 535                 540
Cys Gly Trp Cys Gly Asn Met Cys Gly Gln Gln Lys Glu Cys Pro Gly
545                 550                 555                 560
Ser Trp Gln Gln Asp His Cys Pro Pro Lys Leu Thr Glu Phe His Pro
                565                 570                 575
His Ser Gly Pro Leu Arg Gly Ser Thr Arg Leu Thr Leu Cys Gly Ser
            580                 585                 590
Asn Phe Tyr Leu His Pro Ser Gly Leu Val Pro Glu Gly Thr His Gln
        595                 600                 605
Val Thr Val Gly Gln Ser Pro Cys Arg Pro Leu Pro Lys Asp Ser Ser
    610                 615                 620
Lys Leu Arg Pro Val Pro Arg Lys Asp Phe Val Glu Glu Phe Glu Cys
625                 630                 635                 640
Glu Leu Glu Pro Leu Gly Thr Gln Ala Val Gly Pro Thr Asn Val Ser
                645                 650                 655
Leu Thr Val Thr Asn Met Pro Pro Gly Lys His Phe Arg Val Asp Gly
            660                 665                 670
Thr Ser Val Leu Arg Gly Phe Ser Phe Met Glu Pro Val Leu Ile Ala
        675                 680                 685
Val Gln Pro Leu Phe Gly Pro Arg Ala Gly Gly Thr Cys Leu Thr Leu
    690                 695                 700
Glu Gly Gln Ser Leu Ser Val Gly Thr Ser Arg Ala Val Leu Val Asn
705                 710                 715                 720
Gly Thr Glu Cys Leu Leu Ala Arg Val Ser Glu Gly Gln Leu Leu Cys
                725                 730                 735
Ala Thr Pro Pro Gly Ala Thr Val Ala Ser Val Pro Leu Ser Leu Gln
            740                 745                 750
Val Gly Gly Ala Gln Val Pro Gly Ser Trp Thr Phe Gln Tyr Arg Glu
        755                 760                 765
Asp Pro Val Val Leu Ser Ile Ser Pro Asn Cys Gly Tyr Ile Asn Ser
    770                 775                 780
His Ile Thr Ile Cys Gly Gln His Leu Thr Ser Ala Trp His Leu Val
785                 790                 795                 800
Leu Ser Phe His Asp Gly Leu Arg Ala Val Glu Ser Arg Cys Glu Arg
                805                 810                 815
Gln Leu Pro Glu Gln Gln Leu Cys Arg Leu Pro Glu Tyr Val Val Arg
            820                 825                 830
Asp Pro Gln Gly Trp Val Ala Gly Asn Leu Ser Ala Arg Gly Asp Gly
        835                 840                 845
Ala Ala Gly Phe Thr Leu Pro Gly Phe Arg Phe Leu Pro Pro Pro His
    850                 855                 860
Pro Pro Ser Ala Asn Leu Val Pro Leu Lys Pro Glu Glu His Ala Ile
```

```
865                 870                 875                 880
Lys Phe Glu Tyr Ile Gly Leu Gly Ala Val Ala Asp Cys Val Gly Ile
                885                 890                 895
Asn Val Thr Val Gly Gly Glu Ser Cys Gln His Glu Phe Arg Gly Asp
            900                 905                 910
Met Val Val Cys Pro Leu Pro Pro Ser Leu Gln Leu Gly Gln Asp Gly
        915                 920                 925
Ala Pro Leu Gln Val Cys Val Asp Gly Glu Cys His Ile Leu Gly Arg
    930                 935                 940
Val Val Arg Pro Gly Pro Asp Gly Val Pro Gln Ser Thr Leu Leu Gly
945                 950                 955                 960
Ile Leu Leu Pro Leu Leu Leu Leu Val Ala Ala Leu Ala Thr Ala Leu
                965                 970                 975
Val Phe Ser Tyr Trp Trp Arg Arg Lys Gln Leu Val Leu Pro Pro Asn
            980                 985                 990
Leu Asn Asp Leu Ala Ser Leu Asp Gln Thr Ala Gly Ala Thr Pro Leu
        995                 1000                1005
Pro Ile Leu Tyr Ser Gly Ser Asp Tyr Arg Ser Gly Leu Ala Leu Pro
    1010                1015                1020
Ala Ile Asp Gly Leu Asp Ser Thr Thr Cys Val His Gly Ala Ser Phe
1025                1030                1035                1040
Ser Asp Ser Glu Asp Glu Ser Cys Val Pro Leu Leu Arg Lys Glu Ser
                1045                1050                1055
Ile Gln Leu Arg Asp Leu Asp Ser Ala Leu Leu Ala Glu Val Lys Asp
            1060                1065                1070
Val Leu Ile Pro His Glu Arg Val Val Thr His Ser Asp Arg Val Ile
        1075                1080                1085
Gly Lys Gly His Phe Gly Val Val Tyr His Gly Glu Tyr Ile Asp Gln
    1090                1095                1100
Ala Gln Asn Arg Ile Gln Cys Ala Ile Lys Ser Leu Ser Arg Ile Thr
1105                1110                1115                1120
Glu Met Gln Gln Val Glu Ala Phe Leu Arg Glu Gly Leu Leu Met Arg
                1125                1130                1135
Gly Leu Asn His Pro Asn Val Leu Ala Leu Ile Gly Ile Met Leu Pro
            1140                1145                1150
Pro Glu Gly Leu Pro His Val Leu Leu Pro Tyr Met Cys His Gly Asp
        1155                1160                1165
Leu Leu Gln Phe Ile Arg Ser Pro Gln Arg Asn Pro Thr Val Lys Asp
    1170                1175                1180
Leu Ile Ser Phe Gly Leu Gln Val Ala Arg Gly Met Glu Tyr Leu Ala
1185                1190                1195                1200
Glu Gln Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu
                1205                1210                1215
Asp Glu Ser Phe Thr Val Lys Val Ala Asp Phe Gly Leu Ala Arg Asp
            1220                1225                1230
Ile Leu Asp Arg Glu Tyr Tyr Ser Val Gln Gln His Arg His Ala Arg
        1235                1240                1245
Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr Tyr Arg Phe
    1250                1255                1260
Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Leu
1265                1270                1275                1280
Leu Thr Arg Gly Ala Pro Pro Tyr Arg His Ile Asp Pro Phe Asp Leu
                1285                1290                1295
Thr His Phe Leu Ala Gln Gly Arg Arg Leu Pro Gln Pro Glu Tyr Cys
            1300                1305                1310
Pro Asp Ser Leu Tyr Gln Val Met Gln Gln Cys Trp Glu Ala Asp Pro
```

```
        1315                1320                1325
Ala Val Arg Pro Thr Phe Arg Val Leu Val Gly Glu Val Glu Gln Ile
    1330                1335                1340
Val Ser Ala Leu Leu Gly Asp His Tyr Val Gln Leu Pro Ala Thr Tyr
1345                1350                1355                1360
Met Asn Leu Gly Pro Ser Thr Ser His Glu Met Asn Val Arg Pro Glu
                1365                1370                1375
Gln Pro Gln Phe Ser Pro Met Pro Gly Asn Val Arg Arg Pro Arg Pro
            1380                1385                1390
Leu Ser Glu Pro Pro Arg Pro Thr
        1395                1400


<210> 278
<211> 1124
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP000450
<309> 2004-10-26

<400> 278
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
```

```
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
    290                 295                 300
Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305                 310                 315                 320
Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
                325                 330                 335
Gly Leu Gln Cys Glu Arg Glu Gly Ile Pro Arg Met Thr Pro Lys Ile
            340                 345                 350
Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
        355                 360                 365
Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
    370                 375                 380
Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
385                 390                 395                 400
Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
                405                 410                 415
Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
            420                 425                 430
Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
        435                 440                 445
Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
    450                 455                 460
Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
465                 470                 475                 480
Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
                485                 490                 495
Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
            500                 505                 510
Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly
        515                 520                 525
His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro
    530                 535                 540
Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn
545                 550                 555                 560
Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val
                565                 570                 575
Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys
            580                 585                 590
Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg
        595                 600                 605
Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu
    610                 615                 620
Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro
625                 630                 635                 640
Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val
                645                 650                 655
Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile
            660                 665                 670
Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys
        675                 680                 685
Ile Lys Asn Ala Thr Ile Ile Gln Tyr Gln Leu Lys Gly Leu Glu Pro
    690                 695                 700
Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser
```

```
705                 710                 715                 720
Ser Asn Pro Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln
                725                 730                 735
Ala Pro Ala Asp Leu Gly Gly Gly Lys Met Leu Leu Ile Ala Ile Leu
            740                 745                 750
Gly Ser Ala Gly Met Thr Cys Leu Thr Val Leu Leu Ala Phe Leu Ile
        755                 760                 765
Ile Leu Gln Leu Lys Arg Ala Asn Val Gln Arg Arg Met Ala Gln Ala
    770                 775                 780
Phe Gln Asn Val Arg Glu Glu Pro Ala Val Gln Phe Asn Ser Gly Thr
785                 790                 795                 800
Leu Ala Leu Asn Arg Lys Val Lys Asn Asn Pro Asp Pro Thr Ile Tyr
                805                 810                 815
Pro Val Leu Asp Trp Asn Asp Ile Lys Phe Gln Asp Val Ile Gly Glu
            820                 825                 830
Gly Asn Phe Gly Gln Val Leu Lys Ala Arg Ile Lys Lys Asp Gly Leu
        835                 840                 845
Arg Met Asp Ala Ala Ile Lys Arg Met Lys Glu Tyr Ala Ser Lys Asp
    850                 855                 860
Asp His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly
865                 870                 875                 880
His His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Glu His Arg Gly
                885                 890                 895
Tyr Leu Tyr Leu Ala Ile Glu Tyr Ala Pro His Gly Asn Leu Leu Asp
            900                 905                 910
Phe Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Ile
        915                 920                 925
Ala Asn Ser Thr Ala Ser Thr Leu Ser Ser Gln Gln Leu Leu His Phe
    930                 935                 940
Ala Ala Asp Val Ala Arg Gly Met Asp Tyr Leu Ser Gln Lys Gln Phe
945                 950                 955                 960
Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Gly Glu Asn Tyr
                965                 970                 975
Val Ala Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Gln Glu Val Tyr
            980                 985                 990
Val Lys Lys Thr Met Gly Arg Leu Pro Val Arg Trp Met Ala Ile Glu
        995                 1000                1005
Ser Leu Asn Tyr Ser Val Tyr Thr Thr Asn Ser Asp Val Trp Ser Tyr
    1010                1015                1020
Gly Val Leu Leu Trp Glu Ile Val Ser Leu Gly Gly Thr Pro Tyr Cys
1025                1030                1035                1040
Gly Met Thr Cys Ala Glu Leu Tyr Glu Lys Leu Pro Gln Gly Tyr Arg
                1045                1050                1055
Leu Glu Lys Pro Leu Asn Cys Asp Asp Glu Val Tyr Asp Leu Met Arg
            1060                1065                1070
Gln Cys Trp Arg Glu Lys Pro Tyr Glu Arg Pro Ser Phe Ala Gln Ile
        1075                1080                1085
Leu Val Ser Leu Asn Arg Met Leu Glu Glu Arg Lys Thr Tyr Val Asn
    1090                1095                1100
Thr Thr Leu Tyr Glu Lys Phe Thr Tyr Ala Gly Ile Asp Cys Ser Ala
1105                1110                1115                1120
Glu Glu Ala Ala
```

<210> 279

<211> 1138
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP005415
<309> 2004-12-18

<400> 279
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
1 5 10 15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
20 25 30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
35 40 45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
50 55 60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65 70 75 80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
85 90 95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
100 105 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
115 120 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
130 135 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145 150 155 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
165 170 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
180 185 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
195 200 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
210 215 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225 230 235 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
245 250 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
260 265 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
275 280 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
290 295 300
Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305 310 315 320
Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
325 330 335
Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp Arg Ile Pro Gln
340 345 350
Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu Glu Thr Met Pro
355 360 365
Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser

```
    370                 375                 380
Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Ser Thr Lys Ala
385                 390                 395                 400
Ile Val Glu Pro Glu Lys Thr Thr Ala Glu Phe Glu Val Pro Arg Leu
                405                 410                 415
Val Leu Ala Asp Ser Gly Phe Trp Glu Cys Arg Val Ser Thr Ser Gly
            420                 425                 430
Gly Gln Asp Ser Arg Arg Phe Lys Val Asn Val Lys Val Pro Pro Val
        435                 440                 445
Pro Leu Ala Ala Pro Arg Leu Leu Thr Lys Gln Ser Arg Gln Leu Val
    450                 455                 460
Val Ser Pro Leu Val Ser Phe Ser Gly Asp Gly Pro Ile Ser Thr Val
465                 470                 475                 480
Arg Leu His Tyr Arg Pro Gln Asp Ser Thr Met Asp Trp Ser Thr Ile
                485                 490                 495
Val Val Asp Pro Ser Glu Asn Val Thr Leu Met Asn Leu Arg Pro Lys
            500                 505                 510
Thr Gly Tyr Ser Val Arg Val Gln Leu Ser Arg Pro Gly Glu Gly Gly
        515                 520                 525
Glu Gly Ala Trp Gly Pro Pro Thr Leu Met Thr Thr Asp Cys Pro Glu
    530                 535                 540
Pro Leu Leu Gln Pro Trp Leu Glu Gly Trp His Val Glu Gly Thr Asp
545                 550                 555                 560
Arg Leu Arg Val Ser Trp Ser Leu Pro Leu Val Pro Gly Pro Leu Val
                565                 570                 575
Gly Asp Gly Phe Leu Leu Arg Leu Trp Asp Gly Thr Arg Gly Gln Glu
            580                 585                 590
Arg Arg Glu Asn Val Ser Ser Pro Gln Ala Arg Thr Ala Leu Leu Thr
        595                 600                 605
Gly Leu Thr Pro Gly Thr His Tyr Gln Leu Asp Val Gln Leu Tyr His
    610                 615                 620
Cys Thr Leu Leu Gly Pro Ala Ser Pro Pro Ala His Val Leu Leu Pro
625                 630                 635                 640
Pro Ser Gly Pro Pro Ala Pro Arg His Leu His Ala Gln Ala Leu Ser
                645                 650                 655
Asp Ser Glu Ile Gln Leu Thr Trp Lys His Pro Glu Ala Leu Pro Gly
            660                 665                 670
Pro Ile Ser Lys Tyr Val Val Glu Val Gln Val Ala Gly Gly Ala Gly
        675                 680                 685
Asp Pro Leu Trp Ile Asp Val Asp Arg Pro Glu Glu Thr Ser Thr Ile
    690                 695                 700
Ile Arg Gly Leu Asn Ala Ser Thr Arg Tyr Leu Phe Arg Met Arg Ala
705                 710                 715                 720
Ser Ile Gln Gly Leu Gly Asp Trp Ser Asn Thr Val Glu Glu Ser Thr
                725                 730                 735
Leu Gly Asn Gly Leu Gln Ala Glu Gly Pro Val Gln Glu Ser Arg Ala
            740                 745                 750
Ala Glu Glu Gly Leu Asp Gln Gln Leu Ile Leu Ala Val Val Gly Ser
        755                 760                 765
Val Ser Ala Thr Cys Leu Thr Ile Leu Ala Ala Leu Leu Thr Leu Val
    770                 775                 780
Cys Ile Arg Arg Ser Cys Leu His Arg Arg Arg Thr Phe Thr Tyr Gln
785                 790                 795                 800
Ser Gly Ser Gly Glu Glu Thr Ile Leu Gln Phe Ser Ser Gly Thr Leu
                805                 810                 815
Thr Leu Thr Arg Arg Pro Lys Leu Gln Pro Glu Pro Leu Ser Tyr Pro
```

```
            820                 825                 830
Val Leu Glu Trp Glu Asp Ile Thr Phe Glu Asp Leu Ile Gly Glu Gly
        835                 840                 845
Asn Phe Gly Gln Val Ile Arg Ala Met Ile Lys Lys Asp Gly Leu Lys
    850                 855                 860
Met Asn Ala Ala Ile Lys Met Leu Lys Glu Tyr Ala Ser Glu Asn Asp
865                 870                 875                 880
His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly His
                885                 890                 895
His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Lys Asn Arg Gly Tyr
            900                 905                 910
Leu Tyr Ile Ala Ile Glu Tyr Ala Pro Tyr Gly Asn Leu Leu Asp Phe
        915                 920                 925
Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Arg Glu
    930                 935                 940
His Gly Thr Ala Ser Thr Leu Ser Ser Arg Gln Leu Leu Arg Phe Ala
945                 950                 955                 960
Ser Asp Ala Ala Asn Gly Met Gln Tyr Leu Ser Glu Lys Gln Phe Ile
                965                 970                 975
His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Gly Glu Asn Leu Ala
            980                 985                 990
Ser Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Glu Glu Val Tyr Val
        995                 1000                1005
Lys Lys Thr Met Gly Arg Leu Pro Val Arg Trp Met Ala Ile Glu Ser
    1010                1015                1020
Leu Asn Tyr Ser Val Tyr Thr Thr Lys Ser Asp Val Trp Ser Phe Gly
1025                1030                1035                1040
Val Leu Leu Trp Glu Ile Val Ser Leu Gly Gly Thr Pro Tyr Cys Gly
                1045                1050                1055
Met Thr Cys Ala Glu Leu Tyr Glu Lys Leu Pro Gln Gly Tyr Arg Met
            1060                1065                1070
Glu Gln Pro Arg Asn Cys Asp Asp Glu Val Tyr Glu Leu Met Arg Gln
        1075                1080                1085
Cys Trp Arg Asp Arg Pro Tyr Glu Arg Pro Pro Phe Ala Gln Ile Ala
    1090                1095                1100
Leu Gln Leu Gly Arg Met Leu Glu Ala Arg Lys Ala Tyr Val Asn Met
1105                1110                1115                1120
Ser Leu Phe Glu Asn Phe Thr Tyr Ala Gly Ile Asp Ala Thr Ala Glu
                1125                1130                1135
Glu Ala
```

<210> 280
<211> 455
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP001056
<309> 2004-10-27

<400> 280

```
Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu
 1               5                  10                  15
Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro
```

```
            20                  25                  30
His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys
        35                  40                  45
Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys
    50                  55                  60
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
65                  70                  75                  80
Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu
                85                  90                  95
Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val
            100                 105                 110
Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg
        115                 120                 125
Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe
    130                 135                 140
Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
145                 150                 155                 160
Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu
                165                 170                 175
Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr
            180                 185                 190
Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser
        195                 200                 205
Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu
    210                 215                 220
Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
225                 230                 235                 240
Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu
                245                 250                 255
Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser
            260                 265                 270
Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val
        275                 280                 285
Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys
    290                 295                 300
Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
305                 310                 315                 320
Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn
                325                 330                 335
Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp
            340                 345                 350
Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro
        355                 360                 365
Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu
    370                 375                 380
Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
385                 390                 395                 400
Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala
                405                 410                 415
Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly
            420                 425                 430
Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro
        435                 440                 445
Pro Ala Pro Ser Leu Leu Arg
    450                 455
```

<210> 281
<211> 461
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP001057
<309> 2004-10-26

<400> 281

```
Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
 1               5                  10                  15
Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
            20                  25                  30
Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
        35                  40                  45
Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
    50                  55                  60
Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65                  70                  75                  80
Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
                85                  90                  95
Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
            100                 105                 110
Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
        115                 120                 125
Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
    130                 135                 140
Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
145                 150                 155                 160
Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
                165                 170                 175
Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
            180                 185                 190
Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
        195                 200                 205
Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210                 215                 220
Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225                 230                 235                 240
Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
                245                 250                 255
Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
            260                 265                 270
Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
        275                 280                 285
Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
    290                 295                 300
Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305                 310                 315                 320
Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
                325                 330                 335
Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
            340                 345                 350
Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
```

```
        355                 360                 365
Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
    370                 375                 380
Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385                 390                 395                 400
Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
                405                 410                 415
Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
            420                 425                 430
Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
        435                 440                 445
Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
    450                 455                 460


<210> 282
<211> 1338
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002010
<309> 2004-10-28

<400> 282
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
 1               5                  10                  15
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
```

```
                245                 250                 255
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350
Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365
Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380
Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400
Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415
Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430
Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445
Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460
Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465                 470                 475                 480
Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495
Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510
Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg
        515                 520                 525
Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
    530                 535                 540
Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545                 550                 555                 560
Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
                565                 570                 575
Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
            580                 585                 590
Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
        595                 600                 605
Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met
    610                 615                 620
Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn
625                 630                 635                 640
Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg
                645                 650                 655
Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val
            660                 665                 670
Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro
        675                 680                 685
Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu
```

690 695 700
Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg
705 710 715 720
Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln
725 730 735
Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser
740 745 750
Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr Cys Thr Cys Val Ala
755 760 765
Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Leu Ile Arg Lys Met Lys
770 775 780
Arg Ser Ser Ser Glu Ile Lys Thr Asp Tyr Leu Ser Ile Ile Met Asp
785 790 795 800
Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro Tyr Asp
805 810 815
Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly Lys Ser
820 825 830
Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala Phe Gly
835 840 845
Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys
850 855 860
Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu Leu Lys
865 870 875 880
Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu Leu Gly
885 890 895
Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu Tyr Cys
900 905 910
Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp Leu Phe
915 920 925
Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys Glu Lys
930 935 940
Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp Ser Val
945 950 955 960
Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp Lys Ser
965 970 975
Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr Lys Glu
980 985 990
Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr Ser Phe Gln Val Ala Arg
995 1000 1005
Gly Met Glu Phe Leu Ser Ser Arg Lys Cys Ile His Arg Asp Leu Ala
1010 1015 1020
Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn Val Val Lys Ile Cys Asp
1025 1030 1035 1040
Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn Pro Asp Tyr Val Arg Lys
1045 1050 1055
Gly Asp Thr Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe
1060 1065 1070
Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val Trp Ser Tyr Gly Val Leu
1075 1080 1085
Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser Pro Tyr Pro Gly Val Gln
1090 1095 1100
Met Asp Glu Asp Phe Cys Ser Arg Leu Arg Glu Gly Met Arg Met Arg
1105 1110 1115 1120
Ala Pro Glu Tyr Ser Thr Pro Glu Ile Tyr Gln Ile Met Leu Asp Cys
1125 1130 1135
Trp His Arg Asp Pro Lys Glu Arg Pro Arg Phe Ala Glu Leu Val Glu

```
            1140                1145                1150
Lys Leu Gly Asp Leu Leu Gln Ala Asn Val Gln Gln Asp Gly Lys Asp
        1155                1160                1165
Tyr Ile Pro Ile Asn Ala Ile Leu Thr Gly Asn Ser Gly Phe Thr Tyr
    1170                1175                1180
Ser Thr Pro Ala Phe Ser Glu Asp Phe Phe Lys Glu Ser Ile Ser Ala
1185                1190                1195                1200
Pro Lys Phe Asn Ser Gly Ser Ser Asp Asp Val Arg Tyr Val Asn Ala
                1205                1210                1215
Phe Lys Phe Met Ser Leu Glu Arg Ile Lys Thr Phe Glu Glu Leu Leu
            1220                1225                1230
Pro Asn Ala Thr Ser Met Phe Asp Asp Tyr Gln Gly Asp Ser Ser Thr
        1235                1240                1245
Leu Leu Ala Ser Pro Met Leu Lys Arg Phe Thr Trp Thr Asp Ser Lys
    1250                1255                1260
Pro Lys Ala Ser Leu Lys Ile Asp Leu Arg Val Thr Ser Lys Ser Lys
1265                1270                1275                1280
Glu Ser Gly Leu Ser Asp Val Ser Arg Pro Ser Phe Cys His Ser Ser
                1285                1290                1295
Cys Gly His Val Ser Glu Gly Lys Arg Arg Phe Thr Tyr Asp His Ala
            1300                1305                1310
Glu Leu Glu Arg Lys Ile Ala Cys Cys Ser Pro Pro Pro Asp Tyr Asn
        1315                1320                1325
Ser Val Val Leu Tyr Ser Thr Pro Pro Ile
    1330                1335
```

<210> 283
<211> 1356
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002244
<309> 2004-10-26

<400> 283

```
Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
 1               5                  10                  15
Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
            20                  25                  30
Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
        35                  40                  45
Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
    50                  55                  60
Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65                  70                  75                  80
Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
                85                  90                  95
Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
            100                 105                 110
Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
        115                 120                 125
Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
    130                 135                 140
Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
```

```
145                 150                 155                 160
Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                165                 170                 175
Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
            180                 185                 190
Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
        195                 200                 205
Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220
Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225                 230                 235                 240
Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255
Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270
Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285
Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300
Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320
Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335
Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
            340                 345                 350
Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365
Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
    370                 375                 380
Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400
Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415
Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430
Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445
Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460
Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480
Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495
Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510
Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525
Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540
Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560
Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575
Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590
Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
```

595 600 605
Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
610 615 620
Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625 630 635 640
Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
645 650 655
Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
660 665 670
Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
675 680 685
Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
690 695 700
Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705 710 715 720
Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
725 730 735
Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
740 745 750
Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
755 760 765
Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
770 775 780
Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785 790 795 800
Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
805 810 815
Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp
820 825 830
Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val
835 840 845
Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
850 855 860
Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865 870 875 880
Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
885 890 895
Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
900 905 910
Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
915 920 925
Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
930 935 940
Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys
945 950 955 960
Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
965 970 975
Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
980 985 990
Glu Asp Leu Tyr Lys Asp Phe Leu Thr Leu Glu His Leu Ile Cys Tyr
995 1000 1005
Ser Phe Gln Val Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys
1010 1015 1020
Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn
1025 1030 1035 1040
Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp

```
                1045                1050                1055
Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met
            1060                1065                1070
Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val
        1075                1080                1085
Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser
    1090                1095                1100
Pro Tyr Pro Gly Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys
1105                1110                1115                1120
Glu Gly Thr Arg Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr
                1125                1130                1135
Gln Thr Met Leu Asp Cys Trp His Gly Glu Pro Ser Gln Arg Pro Thr
            1140                1145                1150
Phe Ser Glu Leu Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala
        1155                1160                1165
Gln Gln Asp Gly Lys Asp Tyr Ile Val Leu Pro Ile Ser Glu Thr Leu
    1170                1175                1180
Ser Met Glu Glu Asp Ser Gly Leu Ser Leu Pro Thr Ser Pro Val Ser
1185                1190                1195                1200
Cys Met Glu Glu Glu Glu Val Cys Asp Pro Lys Phe His Tyr Asp Asn
                1205                1210                1215
Thr Ala Gly Ile Ser Gln Tyr Leu Gln Asn Ser Lys Arg Lys Ser Arg
            1220                1225                1230
Pro Val Ser Val Lys Thr Phe Glu Asp Ile Pro Leu Glu Glu Pro Glu
        1235                1240                1245
Val Lys Val Ile Pro Asp Asp Asn Gln Thr Asp Ser Gly Met Val Leu
    1250                1255                1260
Ala Ser Glu Glu Leu Lys Thr Leu Glu Asp Arg Thr Lys Leu Ser Pro
1265                1270                1275                1280
Ser Phe Gly Gly Met Val Pro Ser Lys Ser Arg Glu Ser Val Ala Ser
                1285                1290                1295
Glu Gly Ser Asn Gln Thr Ser Gly Tyr Gln Ser Gly Tyr His Ser Asp
            1300                1305                1310
Asp Thr Asp Thr Thr Val Tyr Ser Ser Glu Glu Ala Glu Leu Leu Lys
        1315                1320                1325
Leu Ile Glu Ile Gly Val Gln Thr Gly Ser Thr Ala Gln Ile Leu Gln
    1330                1335                1340
Pro Asp Ser Gly Thr Thr Leu Ser Ser Pro Pro Val
1345                1350                1355


<210> 284
<211> 1298
<212> PRT
<213> Homo sapiens

<300>
<308> GenBank No. NP002011
<309> 2004-12-18

<400> 284
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
 1               5                  10                  15
Leu Leu Asp Gly Leu Val Ser Asp Tyr Ser Met Thr Pro Pro Thr Leu
            20                  25                  30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
```

```
        35                  40                  45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
    50                  55                  60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65                  70                  75                  80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
                85                  90                  95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
            100                 105                 110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
        115                 120                 125
Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
    130                 135                 140
Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145                 150                 155                 160
Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
                165                 170                 175
Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
            180                 185                 190
Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
        195                 200                 205
Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
    210                 215                 220
Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225                 230                 235                 240
Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
                245                 250                 255
Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
            260                 265                 270
Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
        275                 280                 285
Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
    290                 295                 300
Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305                 310                 315                 320
Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
                325                 330                 335
Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
            340                 345                 350
Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
        355                 360                 365
Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
    370                 375                 380
Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385                 390                 395                 400
Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
                405                 410                 415
Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
            420                 425                 430
Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
        435                 440                 445
Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr
    450                 455                 460
Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465                 470                 475                 480
Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp
```

```
                485                 490                 495
Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
            500                 505                 510
Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
        515                 520                 525
Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
    530                 535                 540
Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile
545                 550                 555                 560
Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
                565                 570                 575
Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
            580                 585                 590
Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
        595                 600                 605
Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
    610                 615                 620
Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
625                 630                 635                 640
Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
                645                 650                 655
Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
            660                 665                 670
Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
        675                 680                 685
Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
    690                 695                 700
His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705                 710                 715                 720
Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
                725                 730                 735
Arg Val Arg Glu Glu Asp Ala Gly Pro Tyr Leu Cys Ser Val Cys Arg
            740                 745                 750
Pro Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser
        755                 760                 765
Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val
    770                 775                 780
Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met
785                 790                 795                 800
Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile
                805                 810                 815
Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser
            820                 825                 830
Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
        835                 840                 845
Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala
    850                 855                 860
Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met
865                 870                 875                 880
Leu Lys Glu Gly Ala Thr Ala Ser Glu Gln Arg Ala Leu Met Ser Glu
                885                 890                 895
Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu
            900                 905                 910
Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu
        915                 920                 925
Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp
```

```
    930                 935                 940
Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe
945                 950                 955                 960
Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser
                965                 970                 975
Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala
            980                 985                 990
Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro
        995                 1000                1005
Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg Gly
    1010                1015                1020
Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala
1025                1030                1035                1040
Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile Cys Asp Phe
                1045                1050                1055
Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
            1060                1065                1070
Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asp
        1075                1080                1085
Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
    1090                1095                1100
Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile
1105                1110                1115                1120
Asn Glu Glu Phe Cys Gln Arg Val Arg Asp Gly Thr Arg Met Arg Ala
                1125                1130                1135
Pro Glu Leu Ala Thr Pro Ala Ile Arg His Ile Met Leu Asn Cys Trp
            1140                1145                1150
Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Asp Leu Val Glu Ile
        1155                1160                1165
Leu Gly Asp Leu Leu Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val
    1170                1175                1180
Cys Met Ala Pro Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser
1185                1190                1195                1200
Gln Val Ser Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp
                1205                1210                1215
Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn
            1220                1225                1230
Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
        1235                1240                1245
Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr Thr
    1250                1255                1260
Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala
1265                1270                1275                1280
Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln Glu Ser Gly
                1285                1290                1295
Phe Arg
```

<210> 285
<211> 972
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT

<222> 279
<223> Xaa = V or M

<220>
<221> VARIANT
<222> 362
<223> Xaa = H or R

<220>
<221> VARIANT
<222> 969
<223> Xaa = Y or C

<400> 285

```
Met Gly Pro Gly Val Leu Leu Leu Leu Leu Val Ala Thr Ala Trp His
 1               5                  10                  15
Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
            20                  25                  30
Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
        35                  40                  45
Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
    50                  55                  60
Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65                  70                  75                  80
Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
                85                  90                  95
Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
            100                 105                 110
Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
        115                 120                 125
Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
    130                 135                 140
Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145                 150                 155                 160
Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
                165                 170                 175
Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
            180                 185                 190
Leu Lys Val Gln Lys Val Ile Pro Gly Pro Pro Ala Leu Thr Leu Val
        195                 200                 205
Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
    210                 215                 220
Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225                 230                 235                 240
Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
                245                 250                 255
Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
            260                 265                 270
Ala Gly Asn Tyr Ser Cys Xaa Ala Ser Asn Val Gln Gly Lys His Ser
        275                 280                 285
Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser
    290                 295                 300
Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305                 310                 315                 320
Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
                325                 330                 335
```

```
Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
            340                 345                 350
Asn Ala Thr Thr Lys Asp Thr Tyr Arg Xaa Thr Phe Thr Leu Ser Leu
        355                 360                 365
Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
    370                 375                 380
Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr
385                 390                 395                 400
Pro Pro Glu Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr
                405                 410                 415
Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
            420                 425                 430
Gln Cys Ser Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
        435                 440                 445
Val Trp Asp Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His
    450                 455                 460
Lys Val Thr Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn
465                 470                 475                 480
Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
                485                 490                 495
Ala Phe Ile Pro Ile Ser Ala Gly Ala His Thr His Pro Pro Asp Glu
            500                 505                 510
Phe Leu Phe Thr Pro Val Val Val Ala Cys Met Ser Ile Met Ala Leu
        515                 520                 525
Leu Leu Leu Leu Leu Leu Leu Leu Leu Tyr Lys Tyr Lys Gln Lys Pro
    530                 535                 540
Lys Tyr Gln Val Arg Trp Lys Ile Ile Glu Ser Tyr Glu Gly Asn Ser
545                 550                 555                 560
Tyr Thr Phe Ile Asp Pro Thr Gln Leu Pro Tyr Asn Glu Lys Trp Glu
                565                 570                 575
Phe Pro Arg Asn Asn Leu Gln Phe Gly Lys Thr Leu Gly Ala Gly Ala
            580                 585                 590
Phe Gly Lys Val Val Glu Ala Thr Ala Phe Gly Leu Gly Lys Glu Asp
        595                 600                 605
Ala Val Leu Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala His Ala
    610                 615                 620
Asp Glu Lys Glu Ala Leu Met Ser Glu Leu Lys Ile Met Ser His Leu
625                 630                 635                 640
Gly Gln His Glu Asn Ile Val Asn Leu Leu Gly Ala Cys Thr His Gly
                645                 650                 655
Gly Pro Val Leu Val Ile Thr Glu Tyr Cys Cys Tyr Gly Asp Leu Leu
            660                 665                 670
Asn Phe Leu Arg Arg Lys Ala Glu Ala Met Leu Gly Pro Ser Leu Ser
        675                 680                 685
Pro Gly Gln Asp Pro Glu Gly Gly Val Asp Tyr Lys Asn Ile His Leu
    690                 695                 700
Glu Lys Lys Tyr Val Arg Arg Asp Ser Gly Phe Ser Ser Gln Gly Val
705                 710                 715                 720
Asp Thr Tyr Val Glu Met Arg Pro Val Ser Thr Ser Ser Asn Asp Ser
                725                 730                 735
Phe Ser Glu Gln Asp Leu Asp Lys Glu Asp Gly Arg Pro Leu Glu Leu
            740                 745                 750
Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
        755                 760                 765
Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
    770                 775                 780
```

```
Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
785                 790                 795                 800
Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
                805                 810                 815
Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
            820                 825                 830
Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
        835                 840                 845
Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
    850                 855                 860
Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
865                 870                 875                 880
Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
                885                 890                 895
Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
            900                 905                 910
Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
        915                 920                 925
Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu
    930                 935                 940
Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
945                 950                 955                 960
Gln Pro Leu Leu Gln Pro Asn Asn Xaa Gln Phe Cys
                965                 970
```

<210> 286
<211> 913
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 53
<223> Xaa = W or A

<220>
<221> VARIANT
<222> 55, 68
<223> Xaa = D or A

<220>
<221> VARIANT
<222> 66, 175
<223> Xaa = S or A

<220>
<221> VARIANT
<222> 105
<223> Xaa = R or A

<220>
<221> VARIANT
<222> 106
<223> Xaa = H or A

<220>
<221> VARIANT
<222> 110
<223> Xaa = L or A

<220>
<221> VARIANT
<222> 112
<223> Xaa = K or A

<220>
<221> VARIANT
<222> 173
<223> Xaa = V or A

<220>
<221> VARIANT
<222> 174
<223> Xaa = M or A

<400> 286

```
Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
 1               5                  10                  15
Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
            20                  25                  30
Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
        35                  40                  45
Ala Ser Ser Ser Xaa Ser Xaa Ser Thr Ala Ala Arg His Ser Arg Leu
    50                  55                  60
Glu Xaa Ser Xaa Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65                  70                  75                  80
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
                85                  90                  95
Val Ala Leu Val Gly Thr Gln Gly Xaa Xaa Ala Gly Gly Xaa Gly Xaa
            100                 105                 110
Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
        115                 120                 125
Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
    130                 135                 140
Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145                 150                 155                 160
Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Xaa Xaa Xaa Val
                165                 170                 175
Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu
            180                 185                 190
Ser Tyr Thr Ala Pro Val Gly Gln Thr Met Tyr Leu Ser Glu Ala Val
        195                 200                 205
Tyr Leu Asn Asp Ser Thr Tyr Asp Gly His Thr Val Gly Gly Leu Gln
    210                 215                 220
Tyr Gly Gly Leu Gly Gln Leu Ala Asp Gly Val Val Gly Leu Asp Asp
225                 230                 235                 240
Phe Arg Lys Ser Gln Glu Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val
                245                 250                 255
Gly Trp Ser Asn His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe
            260                 265                 270
Glu Phe Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Val His Cys Asn
```

```
        275                 280                 285
Asn Met His Thr Leu Gly Ala Arg Leu Pro Gly Gly Val Glu Cys Arg
    290                 295                 300
Phe Arg Arg Gly Pro Ala Met Ala Trp Glu Gly Glu Pro Met Arg His
305                 310                 315                 320
Asn Leu Gly Gly Asn Leu Gly Asp Pro Arg Ala Arg Ala Val Ser Val
                325                 330                 335
Pro Leu Gly Gly Arg Val Ala Arg Phe Leu Gln Cys Arg Phe Leu Phe
            340                 345                 350
Ala Gly Pro Trp Leu Leu Phe Ser Glu Ile Ser Phe Ile Ser Asp Val
        355                 360                 365
Val Asn Asn Ser Ser Pro Ala Leu Gly Gly Thr Phe Pro Pro Ala Pro
    370                 375                 380
Trp Trp Pro Pro Gly Pro Pro Pro Thr Asn Phe Ser Ser Leu Glu Leu
385                 390                 395                 400
Glu Pro Arg Gly Gln Gln Pro Val Ala Lys Ala Glu Gly Ser Pro Thr
                405                 410                 415
Ala Ile Leu Ile Gly Cys Leu Val Ala Ile Ile Leu Leu Leu Leu Leu
            420                 425                 430
Ile Ile Ala Leu Met Leu Trp Arg Leu His Trp Arg Arg Leu Leu Ser
        435                 440                 445
Lys Ala Glu Arg Arg Val Leu Glu Glu Glu Leu Thr Val His Leu Ser
    450                 455                 460
Val Pro Gly Asp Thr Ile Leu Ile Asn Asn Arg Pro Gly Pro Arg Glu
465                 470                 475                 480
Pro Pro Pro Tyr Gln Glu Pro Arg Pro Arg Gly Asn Pro Pro His Ser
                485                 490                 495
Ala Pro Cys Val Pro Asn Gly Ser Ala Leu Leu Leu Ser Asn Pro Ala
            500                 505                 510
Tyr Arg Leu Leu Leu Ala Thr Tyr Ala Arg Pro Pro Arg Gly Pro Gly
        515                 520                 525
Pro Pro Thr Pro Ala Trp Ala Lys Pro Thr Asn Thr Gln Ala Tyr Ser
    530                 535                 540
Gly Asp Tyr Met Glu Pro Glu Lys Pro Gly Ala Pro Leu Leu Pro Pro
545                 550                 555                 560
Pro Pro Gln Asn Ser Val Pro His Tyr Ala Glu Ala Asp Ile Val Thr
                565                 570                 575
Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ala Val Pro Ala Leu Pro
            580                 585                 590
Pro Gly Ala Val Gly Asp Gly Pro Pro Arg Val Asp Phe Pro Arg Ser
        595                 600                 605
Arg Leu Arg Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu Val
    610                 615                 620
His Leu Cys Glu Val Asp Ser Pro Gln Asp Leu Val Ser Leu Asp Phe
625                 630                 635                 640
Pro Leu Asn Val Arg Lys Gly His Pro Leu Leu Val Ala Val Lys Ile
                645                 650                 655
Leu Arg Pro Asp Ala Thr Lys Asn Ala Arg Asn Asp Phe Leu Lys Glu
            660                 665                 670
Val Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile Arg Leu Leu
        675                 680                 685
Gly Val Cys Val Gln Asp Asp Pro Leu Cys Met Ile Thr Asp Tyr Met
    690                 695                 700
Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Ala His Gln Leu Glu Asp
705                 710                 715                 720
Lys Ala Ala Glu Gly Ala Pro Gly Asp Gly Gln Ala Ala Gln Gly Pro
```

```
                725                 730                 735
Thr Ile Ser Tyr Pro Met Leu Leu His Val Ala Ala Gln Ile Ala Ser
            740                 745                 750
Gly Met Arg Tyr Leu Ala Thr Leu Asn Phe Val His Arg Asp Leu Ala
        755                 760                 765
Thr Arg Asn Cys Leu Val Gly Glu Asn Phe Thr Ile Lys Ile Ala Asp
    770                 775                 780
Phe Gly Met Ser Arg Asn Leu Tyr Ala Gly Asp Tyr Tyr Arg Val Gln
785                 790                 795                 800
Gly Arg Ala Val Leu Pro Ile Arg Trp Met Ala Trp Glu Cys Ile Leu
                805                 810                 815
Met Gly Lys Phe Thr Thr Ala Ser Asp Val Trp Ala Phe Gly Val Thr
            820                 825                 830
Leu Trp Glu Val Leu Met Leu Cys Arg Ala Gln Pro Phe Gly Ser Ala
        835                 840                 845
His Arg Arg Ala Gly His Arg Glu Arg Gly Gly Val Leu Pro Gly Pro
    850                 855                 860
Gly Pro Ala Val Tyr Leu Ser Arg Pro Pro Ala Cys Pro Gln Gly Leu
865                 870                 875                 880
Tyr Glu Leu Met Leu Arg Cys Trp Ser Arg Glu Ser Glu Gln Arg Pro
                885                 890                 895
Pro Phe Ser Gln Leu His Arg Phe Leu Ala Glu Asp Ala Leu Asn Thr
            900                 905                 910
Val
```

<210> 287
<211> 855
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 550
<223> Xaa = G or R

```
<400> 287
Met Ile Leu Ile Pro Arg Met Leu Leu Val Leu Phe Leu Leu Leu Pro
 1               5                  10                  15
Ile Leu Ser Ser Ala Lys Ala Gln Val Asn Pro Ala Ile Cys Arg Tyr
            20                  25                  30
Pro Leu Gly Met Ser Gly Gly Gln Ile Pro Asp Glu Asp Ile Thr Ala
        35                  40                  45
Ser Ser Gln Trp Ser Glu Ser Thr Ala Ala Lys Tyr Gly Arg Leu Asp
    50                  55                  60
Ser Glu Glu Gly Asp Gly Ala Trp Cys Pro Glu Ile Pro Val Glu Pro
65                  70                  75                  80
Asp Asp Leu Lys Glu Phe Leu Gln Ile Asp Leu His Thr Leu His Phe
                85                  90                  95
Ile Thr Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly His Gly Ile
            100                 105                 110
Glu Phe Ala Pro Met Tyr Lys Ile Asn Tyr Ser Arg Asp Gly Thr Arg
        115                 120                 125
Trp Ile Ser Trp Arg Asn Arg His Gly Lys Gln Val Leu Asp Gly Asn
    130                 135                 140
```

```
Ser Asn Pro Tyr Asp Ile Phe Leu Lys Asp Leu Glu Pro Pro Ile Val
145                 150                 155                 160
Ala Arg Phe Val Arg Phe Ile Pro Val Thr Asp His Ser Met Asn Val
                165                 170                 175
Cys Met Arg Val Glu Leu Tyr Gly Cys Val Trp Leu Asp Gly Leu Val
            180                 185                 190
Ser Tyr Asn Ala Pro Ala Gly Gln Gln Phe Val Leu Pro Gly Gly Ser
        195                 200                 205
Ile Ile Tyr Leu Asn Asp Ser Val Tyr Asp Gly Ala Val Gly Tyr Ser
    210                 215                 220
Met Thr Glu Gly Leu Gly Gln Leu Thr Asp Gly Val Ser Gly Leu Asp
225                 230                 235                 240
Asp Phe Thr Gln Thr His Glu Tyr His Val Trp Pro Gly Tyr Asp Tyr
                245                 250                 255
Val Gly Trp Arg Asn Glu Ser Ala Thr Asn Gly Tyr Ile Glu Ile Met
            260                 265                 270
Phe Glu Phe Asp Arg Ile Arg Asn Phe Thr Thr Met Lys Val His Cys
        275                 280                 285
Asn Asn Met Phe Ala Lys Gly Val Lys Ile Phe Lys Glu Val Gln Cys
    290                 295                 300
Tyr Phe Arg Ser Glu Ala Ser Glu Trp Glu Pro Asn Ala Ile Ser Phe
305                 310                 315                 320
Pro Leu Val Leu Asp Asp Val Asn Pro Ser Ala Arg Phe Val Thr Val
                325                 330                 335
Pro Leu His His Arg Met Ala Ser Ala Ile Lys Cys Gln Tyr His Phe
            340                 345                 350
Ala Asp Thr Trp Met Met Phe Ser Glu Ile Thr Phe Gln Ser Asp Ala
        355                 360                 365
Ala Met Tyr Asn Asn Ser Glu Ala Leu Pro Thr Ser Pro Met Ala Pro
    370                 375                 380
Thr Thr Tyr Asp Pro Met Leu Lys Val Asp Asp Ser Asn Thr Arg Ile
385                 390                 395                 400
Leu Ile Gly Cys Leu Val Ala Ile Ile Phe Ile Leu Leu Ala Ile Ile
                405                 410                 415
Val Ile Ile Leu Trp Arg Gln Phe Trp Gln Lys Met Leu Glu Lys Ala
            420                 425                 430
Ser Arg Arg Met Leu Asp Asp Glu Met Thr Val Ser Leu Ser Leu Pro
        435                 440                 445
Ser Asp Ser Ser Met Phe Asn Asn Asn Arg Ser Ser Ser Pro Ser Glu
    450                 455                 460
Gln Gly Ser Asn Ser Thr Tyr Asp Arg Ile Phe Pro Leu Arg Pro Asp
465                 470                 475                 480
Tyr Gln Glu Pro Ser Arg Leu Ile Arg Lys Leu Pro Glu Phe Ala Pro
                485                 490                 495
Gly Glu Glu Glu Ser Gly Cys Ser Gly Val Val Lys Pro Val Gln Pro
            500                 505                 510
Ser Gly Pro Glu Gly Val Pro His Tyr Ala Glu Ala Asp Ile Val Asn
        515                 520                 525
Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ser Val Pro Ala Val Thr
    530                 535                 540
Met Asp Leu Leu Ser Xaa Lys Asp Val Ala Val Glu Glu Phe Pro Arg
545                 550                 555                 560
Lys Leu Leu Thr Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu
                565                 570                 575
Val His Leu Cys Glu Val Glu Gly Met Glu Lys Phe Lys Asp Lys Asp
            580                 585                 590
```

```
Phe Ala Leu Asp Val Ser Ala Asn Gln Pro Val Leu Val Ala Val Lys
        595                 600                 605
Met Leu Arg Ala Asp Ala Asn Lys Asn Ala Arg Asn Asp Phe Leu Lys
    610                 615                 620
Glu Ile Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile His Leu
625                 630                 635                 640
Leu Ser Val Cys Ile Thr Asp Asp Pro Leu Cys Met Ile Thr Glu Tyr
                645                 650                 655
Met Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Arg His Glu Pro Pro
            660                 665                 670
Asn Ser Ser Ser Ser Asp Val Arg Thr Val Ser Tyr Thr Asn Leu Lys
        675                 680                 685
Phe Met Ala Thr Gln Ile Ala Ser Gly Met Lys Tyr Leu Ser Ser Leu
    690                 695                 700
Asn Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Lys
705                 710                 715                 720
Asn Tyr Thr Ile Lys Ile Ala Asp Phe Gly Met Ser Arg Asn Leu Tyr
                725                 730                 735
Ser Gly Asp Tyr Tyr Arg Ile Gln Gly Arg Ala Val Leu Pro Ile Arg
            740                 745                 750
Trp Met Ser Trp Glu Ser Ile Leu Leu Gly Lys Phe Thr Thr Ala Ser
        755                 760                 765
Asp Val Trp Ala Phe Gly Val Thr Leu Trp Glu Thr Phe Thr Phe Cys
    770                 775                 780
Gln Glu Gln Pro Tyr Ser Gln Leu Ser Asp Glu Gln Val Ile Glu Asn
785                 790                 795                 800
Thr Gly Glu Phe Phe Arg Asp Gln Gly Arg Gln Thr Tyr Leu Pro Gln
                805                 810                 815
Pro Ala Ile Cys Pro Asp Ser Val Tyr Lys Leu Met Leu Ser Cys Trp
            820                 825                 830
Arg Arg Asp Thr Lys Asn Arg Pro Ser Phe Gln Glu Ile His Leu Leu
        835                 840                 845
Leu Leu Gln Gln Gly Asp Glu
    850                 855


<210> 288
<211> 1210
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 521
<223> Xaa = R or K

<400> 288
Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
 1               5                  10                  15
Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
            20                  25                  30
Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
        35                  40                  45
Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
    50                  55                  60
Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
```

```
65                  70                  75                  80
Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
                85                  90                  95
Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
            100                 105                 110
Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
        115                 120                 125
Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
    130                 135                 140
His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145                 150                 155                 160
Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
                165                 170                 175
Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
            180                 185                 190
Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
        195                 200                 205
Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
    210                 215                 220
Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225                 230                 235                 240
Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255
Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270
Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285
Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300
Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320
Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335
Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350
Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365
Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380
Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400
Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415
Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430
His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445
Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
    450                 455                 460
Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480
Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495
Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
            500                 505                 510
Glu Gly Cys Trp Gly Pro Glu Pro Xaa Asp Cys Val Ser Cys Arg Asn
```

```
        515                 520                 525
Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540
Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560
Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575
Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590
Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605
Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620
Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
625                 630                 635                 640
Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
                645                 650                 655
Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His
            660                 665                 670
Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
        675                 680                 685
Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
    690                 695                 700
Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
705                 710                 715                 720
Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
                725                 730                 735
Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
            740                 745                 750
Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
        755                 760                 765
Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
    770                 775                 780
Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
785                 790                 795                 800
Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
                805                 810                 815
Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
            820                 825                 830
Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
        835                 840                 845
Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
    850                 855                 860
Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
865                 870                 875                 880
Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
                885                 890                 895
Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
            900                 905                 910
Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
        915                 920                 925
Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
    930                 935                 940
Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
945                 950                 955                 960
Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
```

```
                965                 970                 975
Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
            980                 985                 990
Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp
        995                 1000                1005
Asp Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe
    1010                1015                1020
Ser Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala
1025                1030                1035                1040
Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln
                1045                1050                1055
Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp
            1060                1065                1070
Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro
        1075                1080                1085
Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
    1090                1095                1100
Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser
1105                1110                1115                1120
Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
                1125                1130                1135
Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp
            1140                1145                1150
Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp
        1155                1160                1165
Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn
    1170                1175                1180
Gly Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val
1185                1190                1195                1200
Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
                1205                1210
```

<210> 289
<211> 976
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 160
<223> Xaa = A or V

<400> 289

```
Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
 1               5                  10                  15
Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
            20                  25                  30
Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
        35                  40                  45
Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
    50                  55                  60
Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65                  70                  75                  80
Leu Arg Ser Asn Trp Ile Tyr Arg Gly Glu Glu Ala Ser Arg Val His
                85                  90                  95
```

```
Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
                100                 105                 110
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
            115                 120                 125
Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
        130                 135                 140
Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Xaa
145                 150                 155                 160
Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
                165                 170                 175
Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
            180                 185                 190
Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
        195                 200                 205
Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
    210                 215                 220
Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225                 230                 235                 240
Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
                245                 250                 255
Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
            260                 265                 270
Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
        275                 280                 285
Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
    290                 295                 300
Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305                 310                 315                 320
Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
                325                 330                 335
Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
            340                 345                 350
Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
        355                 360                 365
Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
    370                 375                 380
Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Gly Leu Thr
385                 390                 395                 400
Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
                405                 410                 415
Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
            420                 425                 430
His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Glu Ser Leu
        435                 440                 445
Ser Gly Leu Ser Leu Arg Leu Val Lys Lys Glu Pro Arg Gln Leu Glu
    450                 455                 460
Leu Thr Trp Ala Gly Ser Arg Pro Arg Ser Pro Gly Ala Asn Leu Thr
465                 470                 475                 480
Tyr Glu Leu His Val Leu Asn Gln Asp Glu Glu Arg Tyr Gln Met Val
                485                 490                 495
Leu Glu Pro Arg Val Leu Leu Thr Glu Leu Gln Pro Asp Thr Thr Tyr
            500                 505                 510
Ile Val Arg Val Arg Met Leu Thr Pro Leu Gly Pro Gly Pro Phe Ser
        515                 520                 525
Pro Asp His Glu Phe Arg Thr Ser Pro Pro Val Ser Arg Gly Leu Thr
    530                 535                 540
```

```
Gly Gly Glu Ile Val Ala Val Ile Phe Gly Leu Leu Leu Gly Ala Ala
545                 550                 555                 560
Leu Leu Leu Gly Ile Leu Val Phe Arg Ser Arg Arg Ala Gln Arg Gln
                565                 570                 575
Arg Gln Gln Arg Gln Arg Asp Arg Ala Thr Asp Val Asp Arg Glu Asp
            580                 585                 590
Lys Leu Trp Leu Lys Pro Tyr Val Asp Leu Gln Ala Tyr Glu Asp Pro
        595                 600                 605
Ala Gln Gly Ala Leu Asp Phe Thr Arg Glu Leu Asp Pro Ala Trp Leu
    610                 615                 620
Met Val Asp Thr Val Ile Gly Glu Gly Glu Phe Gly Glu Val Tyr Arg
625                 630                 635                 640
Gly Thr Leu Arg Leu Pro Ser Gln Asp Cys Lys Thr Val Ala Ile Lys
                645                 650                 655
Thr Leu Lys Asp Thr Ser Pro Gly Gly Gln Trp Trp Asn Phe Leu Arg
            660                 665                 670
Glu Ala Thr Ile Met Gly Gln Phe Ser His Pro His Ile Leu His Leu
        675                 680                 685
Glu Gly Val Val Thr Lys Arg Lys Pro Ile Met Ile Ile Thr Glu Phe
    690                 695                 700
Met Glu Asn Gly Ala Leu Asp Ala Phe Leu Arg Glu Arg Glu Asp Gln
705                 710                 715                 720
Leu Val Pro Gly Gln Leu Val Ala Met Leu Gln Gly Ile Ala Ser Gly
                725                 730                 735
Met Asn Tyr Leu Ser Asn His Asn Tyr Val His Arg Asp Leu Ala Ala
            740                 745                 750
Arg Asn Ile Leu Val Asn Gln Asn Leu Cys Cys Lys Val Ser Asp Phe
        755                 760                 765
Gly Leu Thr Arg Leu Leu Asp Asp Phe Asp Gly Thr Tyr Glu Thr Gln
    770                 775                 780
Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala His
785                 790                 795                 800
Arg Ile Phe Thr Thr Ala Ser Asp Val Trp Ser Phe Gly Ile Val Met
                805                 810                 815
Trp Glu Val Leu Ser Phe Gly Asp Lys Pro Tyr Gly Glu Met Ser Asn
            820                 825                 830
Gln Glu Val Met Lys Ser Ile Glu Asp Gly Tyr Arg Leu Pro Pro Pro
        835                 840                 845
Val Asp Cys Pro Ala Pro Leu Tyr Glu Leu Met Lys Asn Cys Trp Ala
    850                 855                 860
Tyr Asp Arg Ala Arg Arg Pro His Phe Gln Lys Leu Gln Ala His Leu
865                 870                 875                 880
Glu Gln Leu Leu Ala Asn Pro His Ser Leu Arg Thr Ile Ala Asn Phe
                885                 890                 895
Asp Pro Arg Met Thr Leu Arg Leu Pro Ser Leu Ser Gly Ser Asp Gly
            900                 905                 910
Ile Pro Tyr Arg Thr Val Ser Glu Trp Leu Glu Ser Ile Arg Met Lys
        915                 920                 925
Arg Tyr Ile Leu His Phe His Ser Ala Gly Leu Asp Thr Met Glu Cys
    930                 935                 940
Val Leu Glu Leu Thr Ala Glu Asp Leu Thr Gln Met Gly Ile Thr Leu
945                 950                 955                 960
Pro Gly His Gln Lys Arg Ile Leu Cys Ser Ile Gln Gly Phe Lys Asp
                965                 970                 975
```

<210> 290
<211> 976
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 94
<223> Xaa = I or N

<220>
<221> VARIANT
<222> 96
<223> Xaa = I or F

<220>
<221> VARIANT
<222> 99
<223> Xaa = K or N

<220>
<221> VARIANT
<222> 350
<223> Xaa = P or T

<220>
<221> VARIANT
<222> 825
<223> Xaa = E or K

<400> 290
Met Glu Leu Gln Ala Ala Arg Ala Cys Phe Ala Leu Leu Trp Gly Cys
1 5 10 15
Ala Leu Ala Ala Ala Ala Ala Ala Gln Gly Lys Glu Val Val Leu Leu
20 25 30
Asp Phe Ala Ala Ala Gly Gly Glu Leu Gly Trp Leu Thr His Pro Tyr
35 40 45
Gly Lys Gly Trp Asp Leu Met Gln Asn Ile Met Asn Asp Met Pro Ile
50 55 60
Tyr Met Tyr Ser Val Cys Asn Val Met Ser Gly Asp Gln Asp Asn Trp
65 70 75 80
Leu Arg Thr Asn Trp Val Tyr Arg Gly Glu Ala Glu Arg Xaa Phe Xaa
85 90 95
Glu Leu Xaa Phe Thr Val Arg Asp Cys Asn Ser Phe Pro Gly Gly Ala
100 105 110
Ser Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Ala Glu Ser Asp Leu
115 120 125
Asp Tyr Gly Thr Asn Phe Gln Lys Arg Leu Phe Thr Lys Ile Asp Thr
130 135 140
Ile Ala Pro Asp Glu Ile Thr Val Ser Ser Asp Phe Glu Ala Arg His
145 150 155 160
Val Lys Leu Asn Val Glu Glu Arg Ser Val Gly Pro Leu Thr Arg Lys
165 170 175
Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Val Ala Leu Leu
180 185 190
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Glu Leu Leu Gln Gly Leu

```
        195                 200                 205
Ala His Phe Pro Glu Thr Ile Ala Gly Ser Asp Ala Pro Ser Leu Ala
    210                 215                 220
Thr Val Ala Gly Thr Cys Val Asp His Ala Val Val Pro Pro Gly Gly
225                 230                 235                 240
Glu Glu Pro Arg Met His Cys Ala Val Asp Gly Glu Trp Leu Val Pro
                245                 250                 255
Ile Gly Gln Cys Leu Cys Gln Ala Gly Tyr Glu Lys Val Glu Asp Ala
            260                 265                 270
Cys Gln Ala Cys Ser Pro Gly Phe Phe Lys Phe Glu Ala Ser Glu Ser
        275                 280                 285
Pro Cys Leu Glu Cys Pro Glu His Thr Leu Pro Ser Pro Glu Gly Ala
    290                 295                 300
Thr Ser Cys Glu Cys Glu Glu Gly Phe Phe Arg Ala Pro Gln Asp Pro
305                 310                 315                 320
Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro His Tyr Leu Thr
                325                 330                 335
Ala Val Gly Met Gly Ala Lys Val Glu Leu Arg Trp Thr Xaa Pro Gln
            340                 345                 350
Asp Ser Gly Gly Arg Glu Asp Ile Val Tyr Ser Val Thr Cys Glu Gln
        355                 360                 365
Cys Trp Pro Glu Ser Gly Glu Cys Gly Pro Cys Glu Ala Ser Val Arg
    370                 375                 380
Tyr Ser Glu Pro Pro His Gly Leu Thr Arg Thr Ser Val Thr Val Ser
385                 390                 395                 400
Asp Leu Glu Pro His Met Asn Tyr Thr Phe Thr Val Glu Ala Arg Asn
                405                 410                 415
Gly Val Ser Gly Leu Val Thr Ser Arg Ser Phe Arg Thr Ala Ser Val
            420                 425                 430
Ser Ile Asn Gln Thr Glu Pro Pro Lys Val Arg Leu Glu Gly Arg Ser
        435                 440                 445
Thr Thr Ser Leu Ser Val Ser Trp Ser Ile Pro Pro Pro Gln Gln Ser
    450                 455                 460
Arg Val Trp Lys Tyr Glu Val Thr Tyr Arg Lys Lys Gly Asp Ser Asn
465                 470                 475                 480
Ser Tyr Asn Val Arg Arg Thr Glu Gly Phe Ser Val Thr Leu Asp Asp
                485                 490                 495
Leu Ala Pro Asp Thr Thr Tyr Leu Val Gln Val Gln Ala Leu Thr Gln
            500                 505                 510
Glu Gly Gln Gly Ala Gly Ser Lys Val His Glu Phe Gln Thr Leu Ser
        515                 520                 525
Pro Glu Gly Ser Gly Asn Leu Ala Val Ile Gly Gly Val Ala Val Gly
    530                 535                 540
Val Val Leu Leu Leu Val Leu Ala Gly Val Gly Phe Phe Ile His Arg
545                 550                 555                 560
Arg Arg Lys Asn Gln Arg Ala Arg Gln Ser Pro Glu Asp Val Tyr Phe
                565                 570                 575
Ser Lys Ser Glu Gln Leu Lys Pro Leu Lys Thr Tyr Val Asp Pro His
            580                 585                 590
Thr Tyr Glu Asp Pro Asn Gln Ala Val Leu Lys Phe Thr Thr Glu Ile
        595                 600                 605
His Pro Ser Cys Val Thr Arg Gln Lys Val Ile Gly Ala Gly Glu Phe
    610                 615                 620
Gly Glu Val Tyr Lys Gly Met Leu Lys Thr Ser Ser Gly Lys Lys Glu
625                 630                 635                 640
Val Pro Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Glu Lys Gln
```

```
                645                 650                 655
Arg Val Asp Phe Leu Gly Glu Ala Gly Ile Met Gly Gln Phe Ser His
            660                 665                 670
His Asn Ile Ile Arg Leu Glu Gly Val Ile Ser Lys Tyr Lys Pro Met
        675                 680                 685
Met Ile Ile Thr Glu Tyr Met Glu Asn Gly Ala Leu Asp Lys Phe Leu
    690                 695                 700
Arg Glu Lys Asp Gly Glu Phe Ser Val Leu Gln Leu Val Gly Met Leu
705                 710                 715                 720
Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asn Met Asn Tyr Val
                725                 730                 735
His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val
            740                 745                 750
Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro
        755                 760                 765
Glu Ala Thr Tyr Thr Thr Ser Gly Gly Lys Ile Pro Ile Arg Trp Thr
    770                 775                 780
Ala Pro Glu Ala Ile Ser Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val
785                 790                 795                 800
Trp Ser Phe Gly Ile Val Met Trp Glu Val Met Thr Tyr Gly Glu Arg
                805                 810                 815
Pro Tyr Trp Glu Leu Ser Asn His Xaa Val Met Lys Ala Ile Asn Asp
            820                 825                 830
Gly Phe Arg Leu Pro Thr Pro Met Asp Cys Pro Ser Ala Ile Tyr Gln
        835                 840                 845
Leu Met Met Gln Cys Trp Gln Gln Glu Arg Ala Arg Arg Pro Lys Phe
    850                 855                 860
Ala Asp Ile Val Ser Ile Leu Asp Lys Leu Ile Arg Ala Pro Asp Ser
865                 870                 875                 880
Leu Lys Thr Leu Ala Asp Phe Asp Pro Arg Val Ser Ile Arg Leu Pro
                885                 890                 895
Ser Thr Ser Gly Ser Glu Gly Val Pro Phe Arg Thr Val Ser Glu Trp
            900                 905                 910
Leu Glu Ser Ile Lys Met Gln Gln Tyr Thr Glu His Phe Met Ala Ala
        915                 920                 925
Gly Tyr Thr Ala Ile Glu Lys Val Val Gln Met Thr Asn Asp Asp Ile
    930                 935                 940
Lys Arg Ile Gly Val Arg Leu Pro Gly His Gln Lys Arg Ile Ala Tyr
945                 950                 955                 960
Ser Leu Leu Gly Leu Lys Asp Gln Val Asn Thr Val Gly Ile Pro Ile
                965                 970                 975


<210> 291
<211> 983
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 914
<223> Xaa = R or H

<400> 291
Met Asp Cys Gln Leu Ser Ile Leu Leu Leu Leu Ser Cys Ser Val Leu
 1               5                  10                  15
```

```
Asp Ser Phe Gly Glu Leu Ile Pro Gln Pro Ser Asn Glu Val Asn Leu
            20                  25                  30
Leu Asp Ser Lys Thr Ile Gln Gly Glu Leu Gly Trp Ile Ser Tyr Pro
        35                  40                  45
Ser His Gly Trp Glu Glu Ile Ser Gly Val Asp Glu His Tyr Thr Pro
    50                  55                  60
Ile Arg Thr Tyr Gln Val Cys Asn Val Met Asp His Ser Gln Asn Asn
65                  70                  75                  80
Trp Leu Arg Thr Asn Trp Val Pro Arg Asn Ser Ala Gln Lys Ile Tyr
                85                  90                  95
Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Ile Pro Leu Val
            100                 105                 110
Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp
        115                 120                 125
Asp Asp His Gly Val Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp
    130                 135                 140
Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg
145                 150                 155                 160
Ile Leu Lys Leu Asn Thr Glu Ile Arg Glu Val Gly Pro Val Asn Lys
                165                 170                 175
Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu
            180                 185                 190
Val Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn
        195                 200                 205
Leu Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val
    210                 215                 220
Glu Val Arg Gly Ser Cys Val Asn Asn Ser Lys Glu Glu Asp Pro Pro
225                 230                 235                 240
Arg Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
                245                 250                 255
Cys Ser Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Met Cys Gln Ala
            260                 265                 270
Cys Arg Pro Gly Phe Tyr Lys Ala Leu Asp Gly Asn Met Lys Cys Ala
        275                 280                 285
Lys Cys Pro Pro His Ser Ser Thr Gln Glu Asp Gly Ser Met Asn Cys
    290                 295                 300
Arg Cys Glu Asn Asn Tyr Phe Arg Ala Asp Lys Asp Pro Pro Ser Met
305                 310                 315                 320
Ala Cys Thr Arg Pro Pro Ser Ser Pro Arg Asn Val Ile Ser Asn Ile
                325                 330                 335
Asn Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly
            340                 345                 350
Gly Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Trp
        355                 360                 365
Asn Ile Lys Gln Cys Glu Pro Cys Ser Pro Asn Val Arg Phe Leu Pro
    370                 375                 380
Arg Gln Phe Gly Leu Thr Asn Thr Thr Val Thr Val Thr Asp Leu Leu
385                 390                 395                 400
Ala His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser
                405                 410                 415
Glu Leu Ser Ser Pro Pro Arg Gln Phe Ala Ala Val Ser Ile Thr Thr
            420                 425                 430
Asn Gln Ala Ala Pro Ser Pro Val Leu Thr Ile Lys Lys Asp Arg Thr
        435                 440                 445
Ser Arg Asn Ser Ile Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn
    450                 455                 460
```

```
Gly Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln
465                 470                 475                 480
Glu Thr Ser Tyr Thr Ile Leu Arg Ala Arg Gly Thr Asn Val Thr Ile
                485                 490                 495
Ser Ser Leu Lys Pro Asp Thr Ile Tyr Val Phe Gln Ile Arg Ala Arg
            500                 505                 510
Thr Ala Ala Gly Tyr Gly Thr Asn Ser Arg Lys Phe Glu Phe Glu Thr
        515                 520                 525
Ser Pro Asp Ser Phe Ser Ile Ser Gly Glu Ser Ser Gln Val Val Met
    530                 535                 540
Ile Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Ile
545                 550                 555                 560
Tyr Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Ser Lys His Gly Ala
                565                 570                 575
Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly
            580                 585                 590
Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Thr Gln Ala
        595                 600                 605
Val His Glu Phe Ala Lys Glu Leu Asp Ala Thr Asn Ile Ser Ile Asp
    610                 615                 620
Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625                 630                 635                 640
Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys
                645                 650                 655
Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser
            660                 665                 670
Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val
        675                 680                 685
Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn
    690                 695                 700
Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val
705                 710                 715                 720
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr
                725                 730                 735
Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750
Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765
Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
    770                 775                 780
Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Leu Trp Glu
                805                 810                 815
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Ser Asn Gln Asp
            820                 825                 830
Val Ile Lys Ala Val Asp Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845
Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860
Arg Asn Asn Arg Pro Lys Phe Glu Gln Ile Val Ser Ile Leu Asp Lys
865                 870                 875                 880
Leu Ile Arg Asn Pro Gly Ser Leu Lys Ile Ile Thr Ser Ala Ala Ala
                885                 890                 895
Arg Pro Ser Asn Leu Leu Leu Asp Gln Ser Asn Val Asp Ile Thr Thr
            900                 905                 910
```

```
Phe Xaa Thr Thr Gly Asp Trp Leu Asn Gly Val Trp Thr Ala His Cys
        915                 920                 925
Lys Glu Ile Phe Thr Gly Val Glu Tyr Ser Ser Cys Asp Thr Ile Ala
    930                 935                 940
Lys Ile Ser Thr Asp Asp Met Lys Lys Val Gly Val Thr Val Val Gly
945                 950                 955                 960
Pro Gln Lys Lys Ile Ile Ser Ser Ile Lys Ala Leu Glu Thr Gln Ser
                965                 970                 975
Lys Asn Gly Pro Val Pro Val
            980


<210> 292
<211> 998
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 138
<223> Xaa = I or V

<220>
<221> VARIANT
<222> 278
<223> Xaa = P or S

<400> 292
Met Val Phe Gln Thr Arg Tyr Pro Ser Trp Ile Ile Leu Cys Tyr Ile
 1               5                  10                  15
Trp Leu Leu Arg Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu
            20                  25                  30
Val Leu Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile
        35                  40                  45
Ser Ser Pro Pro Asn Gly Trp Glu Glu Ile Ser Gly Leu Asp Glu Asn
    50                  55                  60
Tyr Thr Pro Ile Arg Thr Tyr Gln Val Cys Gln Val Met Glu Pro Asn
65                  70                  75                  80
Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Ser Lys Gly Asn Ala Gln
                85                  90                  95
Arg Ile Phe Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu
            100                 105                 110
Pro Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr
        115                 120                 125
Glu Thr Asp Tyr Asp Thr Gly Arg Asn Xaa Arg Glu Asn Leu Tyr Val
    130                 135                 140
Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Gly Asp Leu
145                 150                 155                 160
Gly Glu Arg Lys Met Lys Leu Asn Thr Glu Val Arg Glu Ile Gly Pro
                165                 170                 175
Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys
            180                 185                 190
Ile Ala Leu Val Ser Val Lys Val Tyr Tyr Lys Lys Cys Trp Ser Ile
        195                 200                 205
Ile Glu Asn Leu Ala Ile Phe Pro Asp Thr Val Thr Gly Ser Glu Phe
    210                 215                 220
```

```
Ser Ser Leu Val Glu Val Arg Gly Thr Cys Val Ser Ser Ala Glu Glu
225                 230                 235                 240
Glu Ala Glu Asn Ala Pro Arg Met His Cys Ser Ala Glu Gly Glu Trp
                245                 250                 255
Leu Val Pro Ile Gly Lys Cys Ile Cys Lys Ala Gly Tyr Gln Gln Lys
            260                 265                 270
Gly Asp Thr Cys Glu Xaa Cys Gly Arg Gly Phe Tyr Lys Ser Ser Ser
        275                 280                 285
Gln Asp Leu Gln Cys Ser Arg Cys Pro Thr His Ser Phe Ser Asp Lys
    290                 295                 300
Glu Gly Ser Ser Arg Cys Glu Cys Glu Asp Gly Tyr Tyr Arg Ala Pro
305                 310                 315                 320
Ser Asp Pro Pro Tyr Val Ala Cys Thr Arg Pro Pro Ser Ala Pro Gln
                325                 330                 335
Asn Leu Ile Phe Asn Ile Asn Gln Thr Thr Val Ser Leu Glu Trp Ser
            340                 345                 350
Pro Pro Ala Asp Asn Gly Gly Arg Asn Asp Val Thr Tyr Arg Ile Leu
        355                 360                 365
Cys Lys Arg Cys Ser Trp Glu Gln Gly Glu Cys Val Pro Cys Gly Ser
    370                 375                 380
Asn Ile Gly Tyr Met Pro Gln Gln Thr Gly Leu Glu Asp Asn Tyr Val
385                 390                 395                 400
Thr Val Met Asp Leu Leu Ala His Ala Asn Tyr Thr Phe Glu Val Glu
                405                 410                 415
Ala Val Asn Gly Val Ser Asp Leu Ser Arg Ser Gln Arg Leu Phe Ala
            420                 425                 430
Ala Val Ser Ile Thr Thr Gly Gln Ala Ala Pro Ser Gln Val Ser Gly
        435                 440                 445
Val Met Lys Glu Arg Val Leu Gln Arg Ser Val Glu Leu Ser Trp Gln
    450                 455                 460
Glu Pro Glu His Pro Asn Gly Val Ile Thr Glu Tyr Glu Ile Lys Tyr
465                 470                 475                 480
Tyr Glu Lys Asp Gln Arg Glu Arg Thr Tyr Ser Thr Val Lys Thr Lys
                485                 490                 495
Ser Thr Ser Ala Ser Ile Asn Asn Leu Lys Pro Gly Thr Val Tyr Val
            500                 505                 510
Phe Gln Ile Arg Ala Phe Thr Ala Ala Gly Tyr Gly Asn Tyr Ser Pro
        515                 520                 525
Arg Leu Asp Val Ala Thr Leu Glu Glu Ala Thr Gly Lys Met Phe Glu
    530                 535                 540
Ala Thr Ala Val Ser Ser Glu Gln Asn Pro Val Ile Ile Ile Ala Val
545                 550                 555                 560
Val Ala Val Ala Gly Thr Ile Ile Leu Val Phe Met Val Phe Gly Phe
                565                 570                 575
Ile Ile Gly Arg Arg His Cys Gly Tyr Ser Lys Ala Asp Gln Glu Gly
            580                 585                 590
Asp Glu Glu Leu Tyr Phe His Phe Lys Phe Pro Gly Thr Lys Thr Tyr
        595                 600                 605
Ile Asp Pro Glu Thr Tyr Glu Asp Pro Asn Arg Ala Val His Gln Phe
    610                 615                 620
Ala Lys Glu Leu Asp Ala Ser Cys Ile Lys Ile Glu Arg Val Ile Gly
625                 630                 635                 640
Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Gly
                645                 650                 655
Lys Arg Asp Val Ala Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670
```

```
Glu Lys Gln Arg Arg Asp Phe Leu Cys Glu Ala Ser Ile Met Gly Gln
        675                 680                 685
Phe Asp His Pro Asn Val Val His Leu Glu Gly Val Val Thr Arg Gly
    690                 695                 700
Lys Pro Val Met Ile Val Ile Glu Phe Met Glu Asn Gly Ala Leu Asp
705                 710                 715                 720
Ala Phe Leu Arg Lys His Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg Tyr Leu Ala Asp Met
            740                 745                 750
Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Ile Glu
    770                 775                 780
Asp Asp Pro Glu Ala Val Tyr Thr Thr Thr Gly Gly Lys Ile Pro Val
785                 790                 795                 800
Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala
                805                 810                 815
Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr
            820                 825                 830
Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala
        835                 840                 845
Ile Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Asp Cys Pro Ala Gly
    850                 855                 860
Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Glu Arg Ala Glu Arg
865                 870                 875                 880
Pro Lys Phe Glu Gln Ile Val Gly Ile Leu Asp Lys Met Ile Arg Asn
                885                 890                 895
Pro Asn Ser Leu Lys Thr Pro Leu Gly Thr Cys Ser Arg Pro Ile Ser
            900                 905                 910
Pro Leu Leu Asp Gln Asn Thr Pro Asp Phe Thr Thr Phe Cys Ser Val
        915                 920                 925
Gly Glu Trp Leu Gln Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe
    930                 935                 940
Thr Ala Ala Gly Tyr Asn Ser Leu Glu Ser Val Ala Arg Met Thr Ile
945                 950                 955                 960
Glu Asp Val Met Ser Leu Gly Ile Thr Leu Val Gly His Gln Lys Lys
                965                 970                 975
Ile Met Ser Ser Ile Gln Thr Met Arg Ala Gln Met Leu His Leu His
            980                 985                 990
Gly Thr Gly Ile Gln Val
        995
```

<210> 293
<211> 1005
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 301
<223> Xaa = A or V

<220>
<221> VARIANT

<222> 444
<223> Xaa = V or M

<220>
<221> VARIANT
<222> 612
<223> Xaa = E or Q

<400> 293

```
Met Ala Pro Ala Arg Gly Arg Leu Pro Pro Ala Leu Trp Val Val Thr
 1               5                  10                  15
Ala Ala Ala Ala Ala Ala Thr Cys Val Ser Ala Ala Arg Gly Glu Val
            20                  25                  30
Asn Leu Leu Asp Thr Ser Thr Ile His Gly Asp Trp Gly Trp Leu Thr
        35                  40                  45
Tyr Pro Ala His Gly Trp Asp Ser Ile Asn Glu Val Asp Glu Ser Phe
    50                  55                  60
Gln Pro Ile His Thr Tyr Gln Val Cys Asn Val Met Ser Pro Asn Gln
65                  70                  75                  80
Asn Asn Trp Leu Arg Thr Ser Trp Val Pro Arg Asp Gly Ala Arg Arg
                85                  90                  95
Val Tyr Ala Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Met Pro
            100                 105                 110
Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Leu Glu
        115                 120                 125
Ser Asp Arg Asp Leu Gly Ala Ser Thr Gln Glu Ser Gln Phe Leu Lys
    130                 135                 140
Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gly Ala Asp Leu Gly
145                 150                 155                 160
Val Arg Arg Leu Lys Leu Asn Thr Glu Val Arg Ser Val Gly Pro Leu
                165                 170                 175
Ser Lys Arg Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Leu
            180                 185                 190
Ala Ile Leu Ser Leu Arg Ile Tyr Tyr Lys Lys Cys Pro Ala Met Val
        195                 200                 205
Arg Asn Leu Ala Ala Phe Ser Glu Ala Val Thr Gly Ala Asp Ser Ser
    210                 215                 220
Ser Leu Val Glu Val Arg Gly Gln Cys Val Arg His Ser Glu Glu Arg
225                 230                 235                 240
Asp Thr Pro Lys Met Tyr Cys Ser Ala Glu Gly Glu Trp Leu Val Pro
                245                 250                 255
Ile Gly Lys Cys Val Cys Ser Ala Gly Tyr Glu Glu Arg Arg Asp Ala
            260                 265                 270
Cys Val Ala Cys Glu Leu Gly Phe Tyr Lys Ser Ala Pro Gly Asp Gln
        275                 280                 285
Leu Cys Ala Arg Cys Pro Pro His Ser His Ser Ala Xaa Pro Ala Ala
    290                 295                 300
Gln Ala Cys His Cys Asp Leu Ser Tyr Tyr Arg Ala Ala Leu Asp Pro
305                 310                 315                 320
Pro Ser Ser Ala Cys Thr Arg Pro Pro Ser Ala Pro Val Asn Leu Ile
                325                 330                 335
Ser Ser Val Asn Gly Thr Ser Val Thr Leu Glu Trp Ala Pro Pro Leu
            340                 345                 350
Asp Pro Gly Gly Arg Ser Asp Ile Thr Tyr Asn Ala Val Cys Arg Arg
        355                 360                 365
Cys Pro Trp Ala Leu Ser Arg Cys Glu Ala Cys Gly Ser Gly Thr Arg
```

```
    370                 375                 380
Phe Val Pro Gln Gln Thr Ser Leu Val Gln Ala Ser Leu Leu Val Ala
385                 390                 395                 400
Asn Leu Leu Ala His Met Asn Tyr Ser Phe Trp Ile Glu Ala Val Asn
                405                 410                 415
Gly Val Ser Asp Leu Ser Pro Glu Pro Arg Arg Ala Ala Val Val Asn
            420                 425                 430
Ile Thr Thr Asn Gln Ala Ala Pro Ser Gln Val Xaa Val Ile Arg Gln
        435                 440                 445
Glu Arg Ala Gly Gln Thr Ser Val Ser Leu Leu Trp Gln Glu Pro Glu
    450                 455                 460
Gln Pro Asn Gly Ile Ile Leu Glu Tyr Glu Ile Lys Tyr Tyr Glu Lys
465                 470                 475                 480
Asp Lys Glu Met Gln Ser Tyr Ser Thr Leu Lys Ala Val Thr Thr Arg
                485                 490                 495
Ala Thr Val Ser Gly Leu Lys Pro Gly Thr Arg Tyr Val Phe Gln Val
            500                 505                 510
Arg Ala Arg Thr Ser Ala Gly Cys Gly Arg Phe Ser Gln Ala Met Glu
        515                 520                 525
Val Glu Thr Gly Lys Pro Arg Pro Arg Tyr Asp Thr Arg Thr Ile Val
    530                 535                 540
Trp Ile Cys Leu Thr Leu Ile Thr Gly Leu Val Val Leu Leu Leu Leu
545                 550                 555                 560
Leu Ile Cys Lys Lys Arg His Cys Gly Tyr Ser Lys Ala Phe Gln Asp
                565                 570                 575
Ser Asp Glu Glu Lys Met His Tyr Gln Asn Gly Gln Ala Pro Pro Pro
            580                 585                 590
Val Phe Leu Pro Leu His His Pro Pro Gly Lys Leu Pro Glu Pro Gln
        595                 600                 605
Phe Tyr Ala Xaa Pro His Thr Tyr Glu Glu Pro Gly Arg Ala Gly Arg
    610                 615                 620
Ser Phe Thr Arg Glu Ile Glu Ala Ser Arg Ile His Ile Glu Lys Ile
625                 630                 635                 640
Ile Gly Ser Gly Asp Ser Gly Glu Val Cys Tyr Gly Arg Leu Arg Val
                645                 650                 655
Pro Gly Gln Arg Asp Val Pro Val Ala Ile Lys Ala Leu Lys Ala Gly
            660                 665                 670
Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met
        675                 680                 685
Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
    690                 695                 700
Arg Gly Arg Leu Ala Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser
705                 710                 715                 720
Leu Asp Thr Phe Leu Arg Thr His Asp Gly Gln Phe Thr Ile Met Gln
                725                 730                 735
Leu Val Gly Met Leu Arg Gly Val Gly Ala Gly Met Arg Tyr Leu Ser
            740                 745                 750
Asp Leu Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val
        755                 760                 765
Asp Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val
    770                 775                 780
Leu Glu Asp Asp Pro Asp Ala Ala Tyr Thr Thr Thr Gly Gly Lys Ile
785                 790                 795                 800
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Thr Phe Ser
                805                 810                 815
Ser Ala Ser Asp Val Trp Ser Phe Gly Val Val Met Trp Glu Val Leu
```

```
            820                 825                 830
Ala Tyr Gly Glu Arg Pro Tyr Trp Asn Met Thr Asn Arg Asp Val Ile
        835                 840                 845
Ser Ser Val Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Gly Cys Pro
    850                 855                 860
His Ala Leu His Gln Leu Met Leu Asp Cys Trp His Lys Asp Arg Ala
865                 870                 875                 880
Gln Arg Pro Arg Phe Ser Gln Ile Val Ser Val Leu Asp Ala Leu Ile
                885                 890                 895
Arg Ser Pro Glu Ser Leu Arg Ala Thr Ala Thr Val Ser Arg Cys Pro
            900                 905                 910
Pro Pro Ala Phe Val Arg Ser Cys Phe Asp Leu Arg Gly Gly Ser Gly
        915                 920                 925
Gly Gly Gly Gly Leu Thr Val Gly Asp Trp Leu Asp Ser Ile Arg Met
    930                 935                 940
Gly Arg Tyr Arg Asp His Phe Ala Ala Gly Gly Tyr Ser Ser Leu Gly
945                 950                 955                 960
Met Val Leu Arg Met Asn Ala Gln Asp Val Arg Ala Leu Gly Ile Thr
                965                 970                 975
Leu Met Gly His Gln Lys Lys Ile Leu Gly Ser Ile Gln Thr Met Arg
            980                 985                 990
Ala Gln Leu Thr Ser Thr Gln Gly Pro Arg Arg His Leu
        995                 1000                1005
```

<210> 294
<211> 984
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 87
<223> Xaa = T or S

<220>
<221> VARIANT
<222> 152, 367
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 274
<223> Xaa = T or R

<220>
<221> VARIANT
<222> 485
<223> Xaa = R or S

<220>
<221> VARIANT
<222> 813
<223> Xaa = V or I

<220>

<221> VARIANT
<222> 847
<223> Xaa = M or T

<220>
<221> VARIANT
<222> 973
<223> Xaa = R or W

<400> 294

```
Met Ala Leu Asp Tyr Leu Leu Leu Leu Leu Leu Ala Ser Ala Val Ala
 1               5                  10                  15
Ala Met Glu Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu
            20                  25                  30
Gly Trp Thr Ala Asn Pro Ala Ser Gly Trp Glu Glu Val Ser Gly Tyr
        35                  40                  45
Asp Glu Asn Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe
    50                  55                  60
Glu Pro Asn Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg
65                  70                  75                  80
Gly Ala His Arg Ile Tyr Xaa Glu Met Arg Phe Thr Val Arg Asp Cys
                85                  90                  95
Ser Ser Leu Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu
            100                 105                 110
Tyr Tyr Tyr Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe
        115                 120                 125
Trp Ser Glu Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu
    130                 135                 140
Ser Phe Ser Gln Val Asp Phe Xaa Gly Arg Leu Met Lys Val Asn Thr
145                 150                 155                 160
Glu Val Arg Ser Phe Gly Pro Leu Thr Arg Asn Gly Phe Tyr Leu Ala
                165                 170                 175
Phe Gln Asp Tyr Gly Ala Cys Met Ser Leu Leu Ser Val Arg Val Phe
            180                 185                 190
Phe Lys Lys Cys Pro Ser Ile Val Gln Asn Phe Ala Val Phe Pro Glu
        195                 200                 205
Thr Met Thr Gly Ala Glu Ser Thr Ser Leu Val Ile Ala Arg Gly Thr
    210                 215                 220
Cys Ile Pro Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys
225                 230                 235                 240
Asn Gly Asp Gly Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys
                245                 250                 255
Pro Gly Tyr Glu Pro Glu Asn Ser Val Ala Cys Lys Ala Cys Pro Ala
            260                 265                 270
Gly Xaa Phe Lys Ala Ser Gln Glu Ala Glu Gly Cys Ser His Cys Pro
        275                 280                 285
Ser Asn Ser Arg Ser Pro Ala Glu Ala Ser Pro Ile Cys Thr Cys Arg
    290                 295                 300
Thr Gly Tyr Tyr Arg Ala Asp Phe Asp Pro Pro Glu Val Ala Cys Thr
305                 310                 315                 320
Ser Val Pro Ser Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr
                325                 330                 335
Ser Ile Ile Leu Glu Trp His Pro Pro Arg Glu Thr Gly Gly Arg Asp
            340                 345                 350
Asp Val Thr Tyr Asn Ile Ile Cys Lys Lys Cys Arg Ala Asp Xaa Arg
        355                 360                 365
```

```
Ser Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu
    370                 375                 380
Gly Leu Thr Glu Cys Arg Val Ser Ile Ser Ser Leu Trp Ala His Thr
385                 390                 395                 400
Pro Tyr Thr Phe Asp Ile Gln Ala Ile Asn Gly Val Ser Ser Lys Ser
                405                 410                 415
Pro Phe Pro Pro Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala
            420                 425                 430
Ala Pro Ser Thr Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg
        435                 440                 445
Ser Ile Thr Leu Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile
    450                 455                 460
Leu Asp Tyr Glu Ile Arg Tyr Tyr Glu Lys Glu His Asn Glu Phe Asn
465                 470                 475                 480
Ser Ser Met Ala Xaa Ser Gln Thr Asn Thr Ala Arg Ile Asp Gly Leu
                485                 490                 495
Arg Pro Gly Met Val Tyr Val Val Gln Val Arg Ala Arg Thr Val Ala
            500                 505                 510
Gly Tyr Gly Lys Phe Ser Gly Lys Met Cys Phe Gln Thr Leu Thr Asp
        515                 520                 525
Asp Asp Tyr Lys Ser Glu Leu Arg Glu Gln Leu Pro Leu Ile Ala Gly
    530                 535                 540
Ser Ala Ala Ala Gly Val Val Phe Val Val Ser Leu Val Ala Ile Ser
545                 550                 555                 560
Ile Val Cys Ser Arg Lys Arg Ala Tyr Ser Lys Glu Ala Val Tyr Ser
                565                 570                 575
Asp Lys Leu Gln His Tyr Ser Thr Gly Arg Gly Ser Pro Gly Met Lys
            580                 585                 590
Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg
        595                 600                 605
Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Val Lys Ile Glu Glu Val
    610                 615                 620
Ile Gly Ala Gly Glu Phe Gly Glu Val Tyr Lys Gly Arg Leu Lys Leu
625                 630                 635                 640
Pro Gly Lys Arg Glu Ile Tyr Val Ala Ile Lys Thr Leu Lys Ala Gly
                645                 650                 655
Tyr Ser Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met
            660                 665                 670
Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
        675                 680                 685
Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ala
    690                 695                 700
Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln
705                 710                 715                 720
Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala
                725                 730                 735
Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val
            740                 745                 750
Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Tyr
        755                 760                 765
Leu Gln Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly
    770                 775                 780
Lys Ile Pro Val Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Xaa Met Trp Glu
                805                 810                 815
```

```
Val Met Ser Phe Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830
Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Xaa Asp
        835                 840                 845
Cys Pro Ala Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860
Arg Asn Ser Arg Pro Arg Phe Ala Glu Ile Val Asn Thr Leu Asp Lys
865                 870                 875                 880
Met Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr Ala
                885                 890                 895
Val Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr Ala
            900                 905                 910
Phe Thr Thr Val Asp Asp Trp Leu Ser Ala Ile Lys Met Val Gln Tyr
        915                 920                 925
Arg Asp Ser Phe Leu Thr Ala Gly Phe Thr Ser Leu Gln Leu Val Thr
    930                 935                 940
Gln Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Ile Thr Leu Ala Gly
945                 950                 955                 960
His Gln Lys Lys Ile Leu Asn Ser Ile His Ser Met Xaa Val Gln Ile
                965                 970                 975
Ser Gln Ser Pro Thr Ala Met Ala
            980
```

<210> 295
<211> 1055
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 923
<223> Xaa = E or K

<400> 295

```
Met Ala Leu Arg Arg Leu Gly Ala Ala Leu Leu Leu Leu Pro Leu Leu
 1               5                  10                  15
Ala Ala Val Glu Glu Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu
            20                  25                  30
Leu Gly Trp Met Val His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly
        35                  40                  45
Tyr Asp Glu Asn Met Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val
    50                  55                  60
Phe Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Lys Phe Ile Arg Arg
65                  70                  75                  80
Arg Gly Ala His Arg Ile His Val Glu Met Lys Phe Ser Val Arg Asp
                85                  90                  95
Cys Ser Ser Ile Pro Ser Val Pro Gly Ser Cys Lys Glu Thr Phe Asn
            100                 105                 110
Leu Tyr Tyr Tyr Glu Ala Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro
        115                 120                 125
Asn Trp Met Glu Asn Pro Trp Val Lys Val Asp Thr Ile Ala Ala Asp
    130                 135                 140
Glu Ser Phe Ser Gln Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn
145                 150                 155                 160
Thr Glu Val Arg Ser Phe Gly Pro Val Ser Arg Ser Gly Phe Tyr Leu
```

```
                 165                 170                 175
Ala Phe Gln Asp Tyr Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val
            180                 185                 190
Phe Tyr Arg Lys Cys Pro Arg Ile Ile Gln Asn Gly Ala Ile Phe Gln
        195                 200                 205
Glu Thr Leu Ser Gly Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly
    210                 215                 220
Ser Cys Ile Ala Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr
225                 230                 235                 240
Cys Asn Gly Asp Gly Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys
                245                 250                 255
Lys Ala Gly Phe Glu Ala Val Glu Asn Gly Thr Val Cys Arg Gly Cys
            260                 265                 270
Pro Ser Gly Thr Phe Lys Ala Asn Gln Gly Asp Glu Ala Cys Thr His
        275                 280                 285
Cys Pro Ile Asn Ser Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val
    290                 295                 300
Cys Arg Asn Gly Tyr Tyr Arg Ala Asp Leu Asp Pro Leu Asp Met Pro
305                 310                 315                 320
Cys Thr Thr Ile Pro Ser Ala Pro Gln Ala Val Ile Ser Ser Val Asn
                325                 330                 335
Glu Thr Ser Leu Met Leu Glu Trp Thr Pro Pro Arg Asp Ser Gly Gly
            340                 345                 350
Arg Glu Asp Leu Val Tyr Asn Ile Ile Cys Lys Ser Cys Gly Ser Gly
        355                 360                 365
Arg Gly Ala Cys Thr Arg Cys Gly Asp Asn Val Gln Tyr Ala Pro Arg
    370                 375                 380
Gln Leu Gly Leu Thr Glu Pro Arg Ile Tyr Ile Ser Asp Leu Leu Ala
385                 390                 395                 400
His Thr Gln Tyr Thr Phe Glu Ile Gln Ala Val Asn Gly Val Thr Asp
                405                 410                 415
Gln Ser Pro Phe Ser Pro Gln Phe Ala Ser Val Asn Ile Thr Thr Asn
            420                 425                 430
Gln Ala Ala Pro Ser Ala Val Ser Ile Met His Gln Val Ser Arg Thr
        435                 440                 445
Val Asp Ser Ile Thr Leu Ser Trp Ser Gln Pro Asp Gln Pro Asn Gly
    450                 455                 460
Val Ile Leu Asp Tyr Glu Leu Gln Tyr Tyr Glu Lys Glu Leu Ser Glu
465                 470                 475                 480
Tyr Asn Ala Thr Ala Ile Lys Ser Pro Thr Asn Thr Val Thr Val Gln
                485                 490                 495
Gly Leu Lys Ala Gly Ala Ile Tyr Val Phe Gln Val Arg Ala Arg Thr
            500                 505                 510
Val Ala Gly Tyr Gly Arg Tyr Ser Gly Lys Met Tyr Phe Gln Thr Met
        515                 520                 525
Thr Glu Ala Glu Tyr Gln Thr Ser Ile Gln Glu Lys Leu Pro Leu Ile
    530                 535                 540
Ile Gly Ser Ser Ala Ala Gly Leu Val Phe Leu Ile Ala Val Val Val
545                 550                 555                 560
Ile Ala Ile Val Cys Asn Arg Arg Gly Phe Glu Arg Ala Asp Ser Glu
                565                 570                 575
Tyr Thr Asp Lys Leu Gln His Tyr Thr Ser Gly His Met Thr Pro Gly
            580                 585                 590
Met Lys Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala
        595                 600                 605
Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val Lys Ile Glu
```

```
    610                 615                 620
Gln Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly His Leu
625                 630                 635                 640
Lys Leu Pro Gly Lys Arg Glu Ile Phe Val Ala Ile Lys Thr Leu Lys
                645                 650                 655
Ser Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
            660                 665                 670
Ile Met Gly Gln Phe Asp His Pro Asn Val Ile His Leu Glu Gly Val
        675                 680                 685
Val Thr Lys Ser Thr Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn
    690                 695                 700
Gly Ser Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val
705                 710                 715                 720
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr
                725                 730                 735
Leu Ala Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750
Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765
Arg Phe Leu Glu Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ala Leu
    770                 775                 780
Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr
785                 790                 795                 800
Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met
                805                 810                 815
Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn
            820                 825                 830
Gln Asp Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro
        835                 840                 845
Met Asp Cys Pro Ser Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln
    850                 855                 860
Lys Asp Arg Asn His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu
865                 870                 875                 880
Asp Lys Met Ile Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu
                885                 890                 895
Ser Ser Gly Ile Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr
            900                 905                 910
Thr Ser Phe Asn Thr Val Asp Glu Trp Leu Xaa Ala Ile Lys Met Gly
        915                 920                 925
Gln Tyr Lys Glu Ser Phe Ala Asn Ala Gly Phe Thr Ser Phe Asp Val
    930                 935                 940
Val Ser Gln Met Met Met Glu Asp Ile Leu Arg Val Gly Val Thr Leu
945                 950                 955                 960
Ala Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala
                965                 970                 975
Gln Met Asn Gln Ile Gln Ser Val Glu Gly Gln Pro Leu Ala Arg Arg
            980                 985                 990
Pro Arg Ala Thr Gly Arg Thr Lys Arg Cys Gln Pro Arg Asp Val Thr
        995                 1000                1005
Lys Lys Thr Cys Asn Ser Asn Asp Gly Lys Lys Lys Gly Met Gly Lys
    1010                1015                1020
Lys Lys Thr Asp Pro Gly Arg Gly Arg Glu Ile Gln Gly Ile Phe Phe
1025                1030                1035                1040
Lys Glu Asp Ser His Lys Glu Ser Asn Asp Cys Ser Cys Gly Gly
                1045                1050                1055
```

<210> 296
<211> 998
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 981
<223> Xaa = S or I

<400> 296
Met Ala Arg Ala Arg Pro Pro Pro Pro Pro Ser Pro Pro Pro Gly Leu
1 5 10 15
Leu Pro Leu Leu Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Pro
20 25 30
Ala Gly Cys Arg Ala Leu Glu Glu Thr Leu Met Asp Thr Lys Trp Val
35 40 45
Thr Ser Glu Leu Ala Trp Thr Ser His Pro Glu Ser Gly Trp Glu Glu
50 55 60
Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg Thr Tyr Gln Val
65 70 75 80
Cys Asn Val Arg Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Gly Phe
85 90 95
Ile Trp Arg Arg Asp Val Gln Arg Val Tyr Val Glu Leu Lys Phe Thr
100 105 110
Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly Ser Cys Lys Glu
115 120 125
Thr Phe Asn Leu Phe Tyr Tyr Glu Ala Asp Ser Asp Val Ala Ser Ala
130 135 140
Ser Ser Pro Phe Trp Met Glu Asn Pro Tyr Val Lys Val Asp Thr Ile
145 150 155 160
Ala Pro Asp Glu Ser Phe Ser Arg Leu Asp Ala Gly Arg Val Asn Thr
165 170 175
Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu Ala
180 185 190
Phe Gln Asp Gln Gly Ala Cys Met Ser Leu Ile Ser Val Arg Ala Phe
195 200 205
Tyr Lys Lys Cys Ala Ser Thr Thr Ala Gly Phe Ala Leu Phe Pro Glu
210 215 220
Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile Ala Pro Gly Thr
225 230 235 240
Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu Lys Leu Tyr Cys
245 250 255
Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala Cys Thr Cys Ala
260 265 270
Thr Gly His Glu Pro Ala Ala Lys Glu Ser Gln Cys Arg Pro Cys Pro
275 280 285
Pro Gly Ser Tyr Lys Ala Lys Gln Gly Glu Gly Pro Cys Leu Pro Cys
290 295 300
Pro Pro Asn Ser Arg Thr Thr Ser Pro Ala Ala Ser Ile Cys Thr Cys
305 310 315 320
His Asn Asn Phe Tyr Arg Ala Asp Ser Asp Ser Ala Asp Ser Ala Cys
325 330 335
Thr Thr Val Pro Ser Pro Pro Arg Gly Val Ile Ser Asn Val Asn Glu
340 345 350

```
Thr Ser Leu Ile Leu Glu Trp Ser Glu Pro Arg Asp Leu Gly Gly Arg
        355                 360                 365
Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys His Gly Ala Gly
    370                 375                 380
Gly Ala Ser Ala Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro
385                 390                 395                 400
Arg Gln Leu Gly Leu Thr Glu Arg Arg Val His Ile Ser His Leu Leu
                405                 410                 415
Ala His Thr Arg Tyr Thr Phe Glu Val Gln Ala Val Asn Gly Val Ser
            420                 425                 430
Gly Lys Ser Pro Leu Pro Pro Arg Tyr Ala Ala Val Asn Ile Thr Thr
        435                 440                 445
Asn Gln Ala Ala Pro Ser Glu Val Pro Thr Leu Arg Leu His Ser Ser
    450                 455                 460
Ser Gly Ser Ser Leu Thr Leu Ser Trp Ala Pro Pro Glu Arg Pro Asn
465                 470                 475                 480
Gly Val Ile Leu Asp Tyr Glu Met Lys Tyr Phe Glu Lys Ser Glu Gly
                485                 490                 495
Ile Ala Ser Thr Val Thr Ser Gln Met Asn Ser Val Gln Leu Asp Gly
            500                 505                 510
Leu Arg Pro Asp Ala Arg Tyr Val Val Gln Val Arg Ala Arg Thr Val
        515                 520                 525
Ala Gly Tyr Gly Gln Tyr Ser Arg Pro Ala Glu Phe Glu Thr Thr Ser
    530                 535                 540
Glu Arg Gly Ser Gly Ala Gln Gln Leu Gln Glu Gln Leu Pro Leu Ile
545                 550                 555                 560
Val Gly Ser Ala Thr Ala Gly Leu Val Phe Val Val Ala Val Val Val
                565                 570                 575
Ile Ala Ile Val Cys Leu Arg Lys Gln Arg His Gly Ser Asp Ser Glu
            580                 585                 590
Tyr Thr Glu Lys Leu Gln Gln Tyr Ile Ala Pro Gly Met Lys Val Tyr
        595                 600                 605
Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe
    610                 615                 620
Ala Lys Glu Ile Asp Val Ser Cys Val Lys Ile Glu Glu Val Ile Gly
625                 630                 635                 640
Ala Gly Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Gln Pro Gly
                645                 650                 655
Arg Arg Glu Val Phe Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670
Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln
        675                 680                 685
Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Ser
    690                 695                 700
Arg Pro Val Met Ile Leu Thr Glu Phe Met Glu Asn Cys Ala Leu Asp
705                 710                 715                 720
Ser Phe Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735
Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ser Glu Met
            740                 745                 750
Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765
Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu
    770                 775                 780
Asp Asp Pro Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile
785                 790                 795                 800
```

```
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr
                805                 810                 815
Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met
            820                 825                 830
Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile
        835                 840                 845
Asn Ala Val Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro
    850                 855                 860
Thr Ala Leu His Gln Leu Met Leu Asp Cys Trp Val Arg Asp Arg Asn
865                 870                 875                 880
Leu Arg Pro Lys Phe Ser Gln Ile Val Asn Thr Leu Asp Lys Leu Ile
                885                 890                 895
Arg Asn Ala Ala Ser Leu Lys Val Ile Ala Ser Ala Gln Ser Gly Met
            900                 905                 910
Ser Gln Pro Leu Leu Asp Arg Thr Val Pro Asp Tyr Thr Thr Phe Thr
        915                 920                 925
Thr Val Gly Asp Trp Leu Asp Ala Ile Lys Met Gly Arg Tyr Lys Glu
    930                 935                 940
Ser Phe Val Ser Ala Gly Phe Ala Ser Phe Asp Leu Val Ala Gln Met
945                 950                 955                 960
Thr Ala Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln
                965                 970                 975
Lys Lys Ile Leu Xaa Ser Ile Gln Asp Met Arg Leu Gln Met Asn Gln
            980                 985                 990
Thr Leu Pro Val Gln Val
        995


<210> 297
<211> 987
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 463
<223> Xaa = A or D

<220>
<221> VARIANT
<222> 471
<223> Xaa = Y or D

<220>
<221> VARIANT
<222> 926
<223> Xaa = E or D

<400> 297
Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
 1               5                  10                  15
Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
            20                  25                  30
Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
        35                  40                  45
Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
```

```
    50                  55                  60
Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65                  70                  75                  80
Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
                85                  90                  95
Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
            100                 105                 110
Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
        115                 120                 125
Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
    130                 135                 140
His Leu Thr Arg Lys Arg Pro Gly Ala Glu Ala Thr Gly Lys Val Asn
145                 150                 155                 160
Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
                165                 170                 175
Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
            180                 185                 190
Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
        195                 200                 205
Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
    210                 215                 220
Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225                 230                 235                 240
Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
                245                 250                 255
Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Ala Cys Ala
            260                 265                 270
Gln Gly Thr Phe Lys Pro Leu Ser Gly Glu Gly Ser Cys Gln Pro Cys
        275                 280                 285
Pro Ala Asn Ser His Ser Asn Thr Ile Gly Ser Ala Val Cys Gln Cys
    290                 295                 300
Arg Val Gly Tyr Phe Arg Ala Arg Thr Asp Pro Arg Gly Ala Pro Cys
305                 310                 315                 320
Thr Thr Pro Pro Ser Ala Pro Arg Ser Val Val Ser Arg Leu Asn Gly
                325                 330                 335
Ser Ser Leu His Leu Glu Trp Ser Ala Pro Leu Glu Ser Gly Gly Arg
            340                 345                 350
Glu Asp Leu Thr Tyr Ala Leu Arg Cys Arg Glu Cys Arg Pro Gly Gly
        355                 360                 365
Ser Cys Ala Pro Cys Gly Gly Asp Leu Thr Phe Asp Pro Gly Pro Arg
    370                 375                 380
Asp Leu Val Glu Pro Trp Val Val Val Arg Gly Leu Arg Pro Asp Phe
385                 390                 395                 400
Thr Tyr Thr Phe Glu Val Thr Ala Leu Asn Gly Val Ser Ser Leu Ala
                405                 410                 415
Thr Gly Pro Val Pro Phe Glu Pro Val Asn Val Thr Thr Asp Arg Glu
            420                 425                 430
Val Pro Pro Ala Val Ser Asp Ile Arg Val Thr Arg Ser Ser Pro Ser
        435                 440                 445
Ser Leu Ser Leu Ala Trp Ala Val Pro Arg Ala Pro Ser Gly Xaa Val
    450                 455                 460
Leu Asp Tyr Glu Val Lys Xaa His Glu Lys Gly Ala Glu Gly Pro Ser
465                 470                 475                 480
Ser Val Arg Phe Leu Lys Thr Ser Glu Asn Arg Ala Glu Leu Arg Gly
                485                 490                 495
Leu Lys Arg Gly Ala Ser Tyr Leu Val Gln Val Arg Ala Arg Ser Glu
```

```
            500                 505                 510
Ala Gly Tyr Gly Pro Phe Gly Gln Glu His His Ser Gln Thr Gln Leu
        515                 520                 525
Asp Glu Ser Glu Gly Trp Arg Glu Gln Leu Ala Leu Ile Ala Gly Thr
    530                 535                 540
Ala Val Val Gly Val Val Leu Val Leu Val Val Ile Val Val Ala Val
545                 550                 555                 560
Leu Cys Leu Arg Lys Gln Ser Asn Gly Arg Glu Ala Glu Tyr Ser Asp
                565                 570                 575
Lys His Gly Gln Tyr Leu Ile Gly His Gly Thr Lys Val Tyr Ile Asp
            580                 585                 590
Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys
        595                 600                 605
Glu Ile Asp Val Ser Tyr Val Lys Ile Glu Glu Val Ile Gly Ala Gly
    610                 615                 620
Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Ala Pro Gly Lys Lys
625                 630                 635                 640
Glu Ser Cys Val Ala Ile Lys Thr Leu Lys Gly Gly Tyr Thr Glu Arg
                645                 650                 655
Gln Arg Arg Glu Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Glu
            660                 665                 670
His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Asn Ser Met Pro
        675                 680                 685
Val Met Ile Leu Thr Glu Phe Met Glu Asn Gly Ala Leu Asp Ser Phe
    690                 695                 700
Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met
705                 710                 715                 720
Leu Arg Gly Ile Ala Ser Gly Met Arg Tyr Leu Ala Glu Met Ser Tyr
                725                 730                 735
Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu
            740                 745                 750
Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Glu Asn
        755                 760                 765
Ser Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile Pro Ile
    770                 775                 780
Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala
785                 790                 795                 800
Ser Asp Ala Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Phe
                805                 810                 815
Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Asn Ala
            820                 825                 830
Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Pro Asp Cys Pro Thr Ser
        835                 840                 845
Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ala Arg
    850                 855                 860
Pro Arg Phe Pro Gln Val Val Ser Ala Leu Asp Lys Met Ile Arg Asn
865                 870                 875                 880
Pro Ala Ser Leu Lys Ile Val Ala Arg Glu Asn Gly Gly Ala Ser His
                885                 890                 895
Pro Leu Leu Asp Gln Arg Gln Pro His Tyr Ser Ala Phe Gly Ser Val
            900                 905                 910
Gly Glu Trp Leu Arg Ala Ile Lys Met Gly Arg Tyr Glu Xaa Ser Phe
        915                 920                 925
Ala Ala Ala Gly Phe Gly Ser Phe Glu Leu Val Ser Gln Ile Ser Ala
    930                 935                 940
Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln Lys Lys
```

945 950 955 960
Ile Leu Ala Ser Val Gln His Met Lys Ser Gln Ala Lys Pro Gly Thr
965 970 975
Pro Gly Gly Thr Gly Gly Pro Ala Pro Gln Tyr
980 985

<210> 298
<211> 1006
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 107
<223> Xaa = G or S

<220>
<221> VARIANT
<222> 267
<223> Xaa = P or R

<220>
<221> VARIANT
<222> 309
<223> Xaa = S or A

<220>
<221> VARIANT
<222> 484
<223> Xaa = R or Q

<400> 298
Met Val Cys Ser Leu Trp Val Leu Leu Leu Val Ser Ser Val Leu Ala
1 5 10 15
Leu Glu Glu Val Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly
20 25 30
Trp Leu Thr Tyr Pro Pro Gly Gly Trp Asp Glu Val Ser Val Leu Asp
35 40 45
Asp Gln Arg Arg Leu Thr Arg Thr Phe Glu Ala Cys His Val Ala Gly
50 55 60
Ala Pro Pro Gly Thr Gly Gln Asp Asn Trp Leu Gln Thr His Phe Val
65 70 75 80
Glu Arg Arg Gly Ala Gln Arg Ala His Ile Arg Leu His Phe Ser Val
85 90 95
Arg Ala Cys Ser Ser Leu Gly Val Ser Gly Xaa Thr Cys Arg Glu Thr
100 105 110
Phe Thr Leu Tyr Tyr Arg Gln Ala Glu Glu Pro Asp Ser Pro Asp Ser
115 120 125
Val Ser Ser Trp His Leu Lys Arg Trp Thr Lys Val Asp Thr Ile Ala
130 135 140
Ala Asp Glu Ser Phe Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
145 150 155 160
Ser Ala Ala Trp Ala Val Gly Pro His Gly Ala Gly Gln Arg Ala Gly
165 170 175
Leu Gln Leu Asn Val Lys Glu Arg Ser Phe Gly Pro Leu Thr Gln Arg

```
            180                 185                 190
Gly Phe Tyr Val Ala Phe Gln Asp Thr Gly Ala Cys Leu Ala Leu Val
        195                 200                 205
Ala Val Arg Leu Phe Ser Tyr Thr Cys Pro Ala Val Leu Arg Ser Phe
    210                 215                 220
Ala Ser Phe Pro Glu Thr Gln Ala Ser Gly Ala Gly Gly Ala Ser Leu
225                 230                 235                 240
Val Ala Ala Val Gly Thr Cys Val Ala His Ala Glu Pro Glu Glu Asp
                245                 250                 255
Gly Val Gly Gly Gln Ala Gly Gly Ser Pro Xaa Arg Leu His Cys Asn
            260                 265                 270
Gly Glu Gly Lys Trp Met Val Ala Val Gly Gly Cys Arg Cys Gln Pro
        275                 280                 285
Gly Tyr Gln Pro Ala Arg Gly Asp Lys Ala Cys Gln Ala Cys Pro Arg
    290                 295                 300
Gly Leu Tyr Lys Xaa Ser Ala Gly Asn Ala Pro Cys Ser Pro Cys Pro
305                 310                 315                 320
Ala Arg Ser His Ala Pro Asn Pro Ala Ala Pro Val Cys Pro Cys Leu
                325                 330                 335
Glu Gly Phe Tyr Arg Ala Ser Ser Asp Pro Pro Glu Ala Pro Cys Thr
            340                 345                 350
Gly Pro Pro Ser Ala Pro Gln Glu Leu Trp Phe Glu Val Gln Gly Ser
        355                 360                 365
Ala Leu Met Leu His Trp Arg Leu Pro Arg Glu Leu Gly Gly Arg Gly
    370                 375                 380
Asp Leu Leu Phe Asn Val Val Cys Lys Glu Cys Glu Gly Arg Gln Glu
385                 390                 395                 400
Pro Ala Ser Gly Gly Gly Gly Thr Cys His Arg Cys Arg Asp Glu Val
                405                 410                 415
His Phe Asp Pro Arg Gln Arg Gly Leu Thr Glu Ser Arg Val Leu Val
            420                 425                 430
Gly Gly Leu Arg Ala His Val Pro Tyr Ile Leu Glu Val Gln Ala Val
        435                 440                 445
Asn Gly Val Ser Glu Leu Ser Pro Asp Pro Pro Gln Ala Ala Ala Ile
    450                 455                 460
Asn Val Ser Thr Ser His Glu Val Pro Ser Ala Val Pro Val Val His
465                 470                 475                 480
Gln Val Ser Xaa Ala Ser Asn Ser Ile Thr Val Ser Trp Pro Gln Pro
                485                 490                 495
Asp Gln Thr Asn Gly Asn Ile Leu Asp Tyr Gln Leu Arg Tyr Tyr Asp
            500                 505                 510
Gln Ala Glu Asp Glu Ser His Ser Phe Thr Leu Thr Ser Glu Thr Asn
        515                 520                 525
Thr Ala Thr Val Thr Gln Leu Ser Pro Gly His Ile Tyr Gly Phe Gln
    530                 535                 540
Val Arg Ala Arg Thr Ala Ala Gly His Gly Pro Tyr Gly Gly Lys Val
545                 550                 555                 560
Tyr Phe Gln Thr Leu Pro Gln Gly Glu Leu Ser Ser Gln Leu Pro Glu
                565                 570                 575
Arg Leu Ser Leu Val Ile Gly Ser Ile Leu Gly Ala Leu Ala Phe Leu
            580                 585                 590
Leu Leu Ala Ala Ile Thr Val Leu Ala Val Val Phe Gln Arg Lys Arg
        595                 600                 605
Arg Gly Thr Gly Tyr Thr Glu Gln Leu Gln Gln Tyr Ser Ser Pro Gly
    610                 615                 620
Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Cys
```

```
625                 630                 635                 640
Gln Ala Ile Arg Glu Leu Ala Arg Glu Val Asp Pro Ala Tyr Ile Lys
                645                 650                 655
Ile Glu Glu Val Ile Gly Thr Gly Ser Phe Gly Glu Val Arg Gln Gly
            660                 665                 670
Arg Leu Gln Pro Arg Gly Arg Arg Glu Gln Thr Val Ala Ile Gln Ala
        675                 680                 685
Leu Trp Ala Gly Gly Ala Glu Ser Leu Gln Met Thr Phe Leu Gly Arg
    690                 695                 700
Ala Ala Val Leu Gly Gln Phe Gln His Pro Asn Ile Leu Arg Leu Glu
705                 710                 715                 720
Gly Val Val Thr Lys Ser Arg Pro Leu Met Val Leu Thr Glu Phe Met
                725                 730                 735
Glu Leu Gly Pro Leu Asp Ser Phe Leu Arg Gln Arg Glu Gly Gln Phe
            740                 745                 750
Ser Ser Leu Gln Leu Val Ala Met Gln Arg Gly Val Ala Ala Ala Met
        755                 760                 765
Gln Tyr Leu Ser Ser Phe Ala Phe Val His Arg Ser Leu Ser Ala His
    770                 775                 780
Ser Val Leu Val Asn Ser His Leu Val Cys Lys Val Ala Arg Leu Gly
785                 790                 795                 800
His Ser Pro Gln Gly Pro Ser Cys Leu Leu Arg Trp Ala Ala Pro Glu
                805                 810                 815
Val Ile Ala His Gly Lys His Thr Thr Ser Ser Asp Val Trp Ser Phe
            820                 825                 830
Gly Ile Leu Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
        835                 840                 845
Asp Met Ser Glu Gln Glu Val Leu Asn Ala Ile Glu Gln Glu Phe Arg
    850                 855                 860
Leu Pro Pro Pro Pro Gly Cys Pro Pro Gly Leu His Leu Leu Met Leu
865                 870                 875                 880
Asp Thr Trp Gln Lys Asp Arg Ala Arg Arg Pro His Phe Asp Gln Leu
                885                 890                 895
Val Ala Ala Phe Asp Lys Met Ile Arg Lys Pro Asp Thr Leu Gln Ala
            900                 905                 910
Gly Gly Asp Pro Gly Glu Arg Pro Ser Gln Ala Leu Leu Thr Pro Val
        915                 920                 925
Ala Leu Asp Phe Pro Cys Leu Asp Ser Pro Gln Ala Trp Leu Ser Ala
    930                 935                 940
Ile Gly Leu Glu Cys Tyr Gln Asp Asn Phe Ser Lys Phe Gly Leu Cys
945                 950                 955                 960
Thr Phe Ser Asp Val Ala Gln Leu Ser Leu Glu Asp Leu Pro Ala Leu
                965                 970                 975
Gly Ile Thr Leu Ala Gly His Gln Lys Lys Leu Leu His His Ile Gln
            980                 985                 990
Leu Leu Gln Gln His Leu Arg Gln Gln Gly Ser Val Glu Val
        995                 1000                1005
```

<210> 299
<211> 1255
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT

<222> 655
<223> Xaa = I or V

<400> 299

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415
```

```
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
        435                 440                 445
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460
Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495
Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
            500                 505                 510
Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
        515                 520                 525
Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
    530                 535                 540
Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
                565                 570                 575
Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
            580                 585                 590
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605
Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620
Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Xaa Ser
                645                 650                 655
Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
            660                 665                 670
Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
        675                 680                 685
Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
    690                 695                 700
Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720
Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735
Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750
Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765
Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780
Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800
Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815
Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830
Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845
Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860
```

```
Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880
Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895
Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910
Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925
Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940
Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960
Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975
Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990
Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
        995                 1000                1005
Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
    1010                1015                1020
Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025                1030                1035                1040
Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
                1045                1050                1055
Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
            1060                1065                1070
Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
        1075                1080                1085
Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
    1090                1095                1100
Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105                1110                1115                1120
Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
                1125                1130                1135
Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
            1140                1145                1150
Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
        1155                1160                1165
Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
    1170                1175                1180
Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185                1190                1195                1200
Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
                1205                1210                1215
Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
            1220                1225                1230
Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
        1235                1240                1245
Leu Gly Leu Asp Val Pro Val
    1250                1255
```

<210> 300
<211> 820
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 22
<223> Xaa = R or S

<220>
<221> VARIANT
<222> 97, 198
<223> Xaa = G or D

<220>
<221> VARIANT
<222> 99, 275
<223> Xaa = Y or C

<220>
<221> VARIANT
<222> 165
<223> Xaa = A or S

<220>
<221> VARIANT
<222> 190
<223> Xaa = K or E

<220>
<221> VARIANT
<222> 192
<223> Xaa = S or G

<220>
<221> VARIANT
<222> 250
<223> Xaa = P or R

<220>
<221> VARIANT
<222> 605
<223> Xaa = V or M

<220>
<221> VARIANT
<222> 664
<223> Xaa = W or R

<220>
<221> VARIANT
<222> 717
<223> Xaa = M or R

<220>
<221> VARIANT
<222> 770
<223> Xaa = P or S

<220>
<221> VARIANT
<222> 816
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 820
<223> Xaa = R or C

<400> 300
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
1 5 10 15
Thr Leu Cys Thr Ala Xaa Pro Ser Pro Thr Leu Pro Glu Gln Ala Gln
20 25 30
Pro Trp Gly Ala Pro Val Glu Val Glu Ser Phe Leu Val His Pro Gly
35 40 45
Asp Leu Leu Gln Leu Arg Cys Arg Leu Arg Asp Asp Val Gln Ser Ile
50 55 60
Asn Trp Leu Arg Asp Gly Val Gln Leu Ala Glu Ser Asn Arg Thr Arg
65 70 75 80
Ile Thr Gly Glu Glu Val Glu Val Gln Asp Ser Val Pro Ala Asp Ser
85 90 95
Xaa Leu Xaa Ala Cys Val Thr Ser Ser Pro Ser Gly Ser Asp Thr Thr
100 105 110
Tyr Phe Ser Val Asn Val Ser Asp Ala Leu Pro Ser Ser Glu Asp Asp
115 120 125
Asp Asp Asp Asp Asp Ser Ser Ser Glu Glu Lys Glu Thr Asp Asn Thr
130 135 140
Lys Pro Asn Pro Val Ala Pro Tyr Trp Thr Ser Pro Glu Lys Met Glu
145 150 155 160
Lys Lys Leu His Xaa Val Pro Ala Ala Lys Thr Val Lys Phe Lys Cys
165 170 175
Pro Ser Ser Gly Thr Pro Asn Pro Thr Leu Arg Trp Leu Xaa Asn Xaa
180 185 190
Lys Glu Phe Lys Pro Xaa His Arg Ile Gly Gly Tyr Lys Val Arg Tyr
195 200 205
Ala Thr Trp Ser Ile Ile Met Asp Ser Val Val Pro Ser Asp Lys Gly
210 215 220
Asn Tyr Thr Cys Ile Val Glu Asn Glu Tyr Gly Ser Ile Asn His Thr
225 230 235 240
Tyr Gln Leu Asp Val Val Glu Arg Ser Xaa His Arg Pro Ile Leu Gln
245 250 255
Ala Gly Leu Pro Ala Asn Lys Thr Val Ala Leu Gly Ser Asn Val Glu
260 265 270
Phe Met Xaa Lys Val Tyr Ser Asp Pro Gln Pro His Ile Gln Trp Leu
275 280 285
Lys His Ile Glu Val Asn Gly Ser Lys Ile Gly Pro Asp Asn Leu Pro
290 295 300
Tyr Val Gln Ile Leu Lys Thr Ala Gly Val Asn Thr Thr Asp Lys Glu
305 310 315 320
Met Glu Val Leu His Leu Arg Asn Val Ser Phe Glu Asp Ala Gly Glu
325 330 335
Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser His His Ser Ala
340 345 350
Trp Leu Thr Val Leu Glu Ala Leu Glu Glu Arg Pro Ala Val Met Thr

```
        355                 360                 365
Ser Pro Leu Tyr Leu Glu Ile Ile Ile Tyr Cys Thr Gly Ala Phe Leu
    370                 375                 380
Ile Ser Cys Met Val Gly Ser Val Ile Val Tyr Lys Met Lys Ser Gly
385                 390                 395                 400
Thr Lys Lys Ser Asp Phe His Ser Gln Met Ala Val His Lys Leu Ala
                405                 410                 415
Lys Ser Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala Asp Ser Ser
            420                 425                 430
Ala Ser Met Asn Ser Gly Val Leu Leu Val Arg Pro Ser Arg Leu Ser
        435                 440                 445
Ser Ser Gly Thr Pro Met Leu Ala Gly Val Ser Glu Tyr Glu Leu Pro
    450                 455                 460
Glu Asp Pro Arg Trp Glu Leu Pro Arg Asp Arg Leu Val Leu Gly Lys
465                 470                 475                 480
Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val Leu Ala Glu Ala Ile
                485                 490                 495
Gly Leu Asp Lys Asp Lys Pro Asn Arg Val Thr Lys Val Ala Val Lys
            500                 505                 510
Met Leu Lys Ser Asp Ala Thr Glu Lys Asp Leu Ser Asp Leu Ile Ser
        515                 520                 525
Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn
    530                 535                 540
Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val Ile Val Glu
545                 550                 555                 560
Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Gln Ala Arg Arg Pro
                565                 570                 575
Pro Gly Leu Glu Tyr Cys Tyr Asn Pro Ser His Asn Pro Glu Glu Gln
            580                 585                 590
Leu Ser Ser Lys Asp Leu Val Ser Cys Ala Tyr Gln Xaa Ala Arg Gly
        595                 600                 605
Met Glu Tyr Leu Ala Ser Lys Lys Cys Ile His Arg Asp Leu Ala Ala
    610                 615                 620
Arg Asn Val Leu Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe
625                 630                 635                 640
Gly Leu Ala Arg Asp Ile His His Ile Asp Tyr Tyr Lys Lys Thr Thr
                645                 650                 655
Asn Gly Arg Leu Pro Val Lys Xaa Met Ala Pro Glu Ala Leu Phe Asp
            660                 665                 670
Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
        675                 680                 685
Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly Val Pro Val
    690                 695                 700
Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His Arg Xaa Asp Lys Pro
705                 710                 715                 720
Ser Asn Cys Thr Asn Glu Leu Tyr Met Met Met Arg Asp Cys Trp His
                725                 730                 735
Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu
            740                 745                 750
Asp Arg Ile Val Ala Leu Thr Ser Asn Gln Glu Tyr Leu Asp Leu Ser
        755                 760                 765
Met Xaa Leu Asp Gln Tyr Ser Pro Ser Phe Pro Asp Thr Arg Ser Ser
    770                 775                 780
Thr Cys Ser Ser Gly Glu Asp Ser Val Phe Ser His Glu Pro Leu Pro
785                 790                 795                 800
Glu Glu Pro Cys Leu Pro Arg His Pro Ala Gln Leu Ala Asn Gly Xaa
```

805 810 815
Leu Lys Arg Xaa
820

<210> 301
<211> 821
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 6
<223> Xaa = R or P

<220>
<221> VARIANT
<222> 20
<223> Xaa = W or C

<220>
<221> VARIANT
<222> 31
<223> Xaa = T or I

<220>
<221> VARIANT
<222> 105
<223> Xaa = Y or C

<220>
<221> VARIANT
<222> 152, 338, 384, 678
<223> Xaa = R or G

<220>
<221> VARIANT
<222> 162, 186
<223> Xaa = M or T

<220>
<221> VARIANT
<222> 172
<223> Xaa = A or F

<220>
<221> VARIANT
<222> 252
<223> Xaa = S or W or L

<220>
<221> VARIANT
<222> 253
<223> Xaa = P or S or F

<220>

<221> VARIANT
<222> 267
<223> Xaa = S or P

<220>
<221> VARIANT
<222> 276
<223> Xaa = F or V

<220>
<221> VARIANT
<222> 278
<223> Xaa = C or F

<220>
<221> VARIANT
<222> 281
<223> Xaa = Y or C

<220>
<221> VARIANT
<222> 289
<223> Xaa = Q or P

<220>
<221> VARIANT
<222> 315
<223> Xaa = A or S

<220>
<221> VARIANT
<222> 340
<223> Xaa = Y or H

<220>
<221> VARIANT
<222> 341
<223> Xaa = T or P

<220>
<221> VARIANT
<222> 342
<223> Xaa = C or R or Y or S or F or W

<220>
<221> VARIANT
<222> 344
<223> Xaa = A or P or G

<220>
<221> VARIANT
<222> 347, 351, 372
<223> Xaa = S or C

<220>
<221> VARIANT

<222> 443
<223> Xaa = P or A

<220>
<221> VARIANT
<222> 549
<223> Xaa = N or H

<220>
<221> VARIANT
<222> 565
<223> Xaa = E or G

<220>
<221> VARIANT
<222> 641
<223> Xaa = K or R

<220>
<221> VARIANT
<222> 659
<223> Xaa = K or N

<220>
<221> VARIANT
<222> 663
<223> Xaa = G or E

<400> 301

```
Met Val Ser Trp Gly Xaa Phe Ile Cys Leu Val Val Val Thr Met Ala
 1               5                  10                  15
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Xaa Thr
            20                  25                  30
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
        35                  40                  45
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
    50                  55                  60
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65                  70                  75                  80
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
                85                  90                  95
Ala Thr Pro Arg Asp Ser Gly Leu Xaa Ala Cys Thr Ala Ser Arg Thr
            100                 105                 110
Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
        115                 120                 125
Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
    130                 135                 140
Ser Glu Asn Ser Asn Asn Lys Xaa Ala Pro Tyr Trp Thr Asn Thr Glu
145                 150                 155                 160
Lys Xaa Glu Lys Arg Leu His Ala Val Pro Ala Xaa Asn Thr Val Lys
                165                 170                 175
Phe Arg Cys Pro Ala Gly Gly Asn Pro Xaa Pro Thr Met Arg Trp Leu
            180                 185                 190
Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
        195                 200                 205
Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
```

```
    210                 215                 220
Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225                 230                 235                 240
Asn His Thr Tyr His Leu Asp Val Val Glu Arg Xaa Xaa His Arg Pro
                245                 250                 255
Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Xaa Thr Val Val Gly Gly
            260                 265                 270
Asp Val Glu Xaa Val Xaa Lys Val Xaa Ser Asp Ala Gln Pro His Ile
        275                 280                 285
Xaa Xaa Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
    290                 295                 300
Gly Leu Pro Tyr Leu Lys Val Leu Lys Ala Xaa Gly Val Asn Thr Thr
305                 310                 315                 320
Asp Lys Glu Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe Glu Asp
                325                 330                 335
Ala Xaa Glu Xaa Xaa Xaa Leu Xaa Gly Asn Xaa Ile Gly Ile Xaa Phe
            340                 345                 350
His Ser Ala Trp Leu Thr Val Leu Pro Ala Pro Gly Arg Glu Lys Glu
        355                 360                 365
Ile Thr Ala Xaa Pro Asp Xaa Leu Glu Ile Ala Ile Tyr Cys Ile Xaa
    370                 375                 380
Val Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg Met
385                 390                 395                 400
Lys Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val His
                405                 410                 415
Lys Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala
            420                 425                 430
Glu Ser Ser Ser Ser Met Asn Ser Asn Thr Xaa Leu Val Arg Ile Thr
        435                 440                 445
Thr Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val Ser
    450                 455                 460
Glu Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp Lys
465                 470                 475                 480
Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val
                485                 490                 495
Met Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala Val
            500                 505                 510
Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp Leu
        515                 520                 525
Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His
    530                 535                 540
Lys Asn Ile Ile Xaa Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu
545                 550                 555                 560
Tyr Val Ile Val Xaa Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu
                565                 570                 575
Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg
            580                 585                 590
Val Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr
        595                 600                 605
Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His
    610                 615                 620
Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met
625                 630                 635                 640
Xaa Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr
                645                 650                 655
Tyr Lys Xaa Thr Thr Asn Xaa Arg Leu Pro Val Lys Trp Met Ala Pro
```

```
            660                 665                 670
Glu Ala Leu Phe Asp Xaa Val Tyr Thr His Gln Ser Asp Val Trp Ser
        675                 680                 685
Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr
    690                 695                 700
Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His
705                 710                 715                 720
Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met Met
                725                 730                 735
Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln
            740                 745                 750
Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu Glu
        755                 760                 765
Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr Pro
    770                 775                 780
Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser Pro
785                 790                 795                 800
Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile Asn
                805                 810                 815
Gly Ser Val Lys Thr
            820
```

<210> 302
<211> 806
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 65
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 250
<223> Xaa = P or R

<220>
<221> VARIANT
<222> 383
<223> Xaa = F or C

<400> 302

```
Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile
 1               5                  10                  15
Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val
            20                  25                  30
Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln
        35                  40                  45
Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro
    50                  55                  60
Xaa Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly
65                  70                  75                  80
Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val
                85                  90                  95
```

```
Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg
            100                 105                 110
Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala
        115                 120                 125
Pro Ser Ser Gly Asp Asp Glu Asp Gly Glu Asp Glu Ala Glu Asp Thr
    130                 135                 140
Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp
145                 150                 155                 160
Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys
                165                 170                 175
Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly
            180                 185                 190
Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His
        195                 200                 205
Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly
    210                 215                 220
Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr
225                 230                 235                 240
Tyr Thr Leu Asp Val Leu Glu Arg Ser Xaa His Arg Pro Ile Leu Gln
                245                 250                 255
Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu
            260                 265                 270
Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu
        275                 280                 285
Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro
    290                 295                 300
Tyr Val Thr Val Leu Lys Thr Ala Gly Ala Asn Thr Thr Asp Lys Glu
305                 310                 315                 320
Leu Glu Val Leu Ser Leu His Asn Val Thr Phe Glu Asp Ala Gly Glu
                325                 330                 335
Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Phe Ser His His Ser Ala
            340                 345                 350
Trp Leu Val Val Leu Pro Ala Glu Glu Glu Leu Val Glu Ala Asp Glu
        355                 360                 365
Ala Gly Ser Val Tyr Ala Gly Ile Leu Ser Tyr Gly Val Gly Xaa Phe
    370                 375                 380
Leu Phe Ile Leu Val Val Ala Ala Val Thr Leu Cys Arg Leu Arg Ser
385                 390                 395                 400
Pro Pro Lys Lys Gly Leu Gly Ser Pro Thr Val His Lys Ile Ser Arg
                405                 410                 415
Phe Pro Leu Lys Arg Gln Val Ser Leu Glu Ser Asn Ala Ser Met Ser
            420                 425                 430
Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly
        435                 440                 445
Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys
    450                 455                 460
Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu
465                 470                 475                 480
Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys
                485                 490                 495
Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp
            500                 505                 510
Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met
        515                 520                 525
Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala
    530                 535                 540
```

```
Cys Thr Gln Gly Gly Pro Leu Tyr Val Leu Val Glu Tyr Ala Ala Lys
545                 550                 555                 560
Gly Asn Leu Arg Glu Phe Leu Arg Ala Arg Arg Pro Pro Gly Leu Asp
                565                 570                 575
Tyr Ser Phe Asp Thr Cys Lys Pro Pro Glu Glu Gln Leu Thr Phe Lys
            580                 585                 590
Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu
        595                 600                 605
Ala Ser Gln Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu
    610                 615                 620
Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg
625                 630                 635                 640
Asp Val His Asn Leu Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu
                645                 650                 655
Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr
            660                 665                 670
His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe
        675                 680                 685
Thr Leu Gly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe
    690                 695                 700
Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn Cys Thr
705                 710                 715                 720
His Asp Leu Tyr Met Ile Met Arg Glu Cys Trp His Ala Ala Pro Ser
                725                 730                 735
Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Val Leu
            740                 745                 750
Thr Val Thr Ser Thr Asp Glu Tyr Leu Asp Leu Ser Ala Pro Phe Glu
        755                 760                 765
Gln Tyr Ser Pro Gly Gly Gln Asp Thr Pro Ser Ser Ser Ser Ser Gly
    770                 775                 780
Asp Asp Ser Val Phe Ala His Asp Leu Leu Pro Pro Ala Pro Pro Ser
785                 790                 795                 800
Ser Gly Gly Ser Arg Thr
                805
```

<210> 303
<211> 802
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 10
<223> Xaa = V or I

<220>
<221> VARIANT
<222> 136
<223> Xaa = P or L

<220>
<221> VARIANT
<222> 275
<223> Xaa = S or R

<220>
<221> VARIANT
<222> 297
<223> Xaa = D or V

<220>
<221> VARIANT
<222> 388
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 616
<223> Xaa = R or L

<400> 303

```
Met Arg Leu Leu Leu Ala Leu Leu Gly Xaa Leu Leu Ser Val Pro Gly
 1               5                  10                  15
Pro Pro Val Leu Ser Leu Glu Ala Ser Glu Glu Val Glu Leu Glu Pro
            20                  25                  30
Cys Leu Ala Pro Ser Leu Glu Gln Gln Glu Gln Glu Leu Thr Val Ala
        35                  40                  45
Leu Gly Gln Pro Val Arg Leu Cys Cys Gly Arg Ala Glu Arg Gly Gly
    50                  55                  60
His Trp Tyr Lys Glu Gly Ser Arg Leu Ala Pro Ala Gly Arg Val Arg
65                  70                  75                  80
Gly Trp Arg Gly Arg Leu Glu Ile Ala Ser Phe Leu Pro Glu Asp Ala
                85                  90                  95
Gly Arg Tyr Leu Cys Leu Ala Arg Gly Ser Met Ile Val Leu Gln Asn
            100                 105                 110
Leu Thr Leu Ile Thr Gly Asp Ser Leu Thr Ser Ser Asn Asp Asp Glu
        115                 120                 125
Asp Pro Lys Ser His Arg Asp Xaa Ser Asn Arg His Ser Tyr Pro Gln
    130                 135                 140
Gln Ala Pro Tyr Trp Thr His Pro Gln Arg Met Glu Lys Lys Leu His
145                 150                 155                 160
Ala Val Pro Ala Gly Asn Thr Val Lys Phe Arg Cys Pro Ala Ala Gly
                165                 170                 175
Asn Pro Thr Pro Thr Ile Arg Trp Leu Lys Asp Gly Gln Ala Phe His
            180                 185                 190
Gly Glu Asn Arg Ile Gly Gly Ile Arg Leu Arg His Gln His Trp Ser
        195                 200                 205
Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly Thr Tyr Thr Cys
    210                 215                 220
Leu Val Glu Asn Ala Val Gly Ser Ile Arg Tyr Asn Tyr Leu Leu Asp
225                 230                 235                 240
Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro
                245                 250                 255
Ala Asn Thr Thr Ala Val Val Gly Ser Asp Val Glu Leu Leu Cys Lys
            260                 265                 270
Val Tyr Xaa Asp Ala Gln Pro His Ile Gln Trp Leu Lys His Ile Val
        275                 280                 285
Ile Asn Gly Ser Ser Phe Gly Ala Xaa Gly Phe Pro Tyr Val Gln Val
    290                 295                 300
Leu Lys Thr Ala Asp Ile Asn Ser Ser Glu Val Glu Val Leu Tyr Leu
305                 310                 315                 320
```

```
Arg Asn Val Ser Ala Glu Asp Ala Gly Glu Tyr Thr Cys Leu Ala Gly
                325                 330                 335
Asn Ser Ile Gly Leu Ser Tyr Gln Ser Ala Trp Leu Thr Val Leu Pro
            340                 345                 350
Glu Glu Asp Pro Thr Trp Thr Ala Ala Ala Pro Glu Ala Arg Tyr Thr
        355                 360                 365
Asp Ile Ile Leu Tyr Ala Ser Gly Ser Leu Ala Leu Ala Val Leu Leu
    370                 375                 380
Leu Leu Ala Xaa Leu Tyr Arg Gly Gln Ala Leu His Gly Arg His Pro
385                 390                 395                 400
Arg Pro Pro Ala Thr Val Gln Lys Leu Ser Arg Phe Pro Leu Ala Arg
                405                 410                 415
Gln Phe Ser Leu Glu Ser Gly Ser Ser Gly Lys Ser Ser Ser Ser Leu
            420                 425                 430
Val Arg Gly Val Arg Leu Ser Ser Ser Gly Pro Ala Leu Leu Ala Gly
        435                 440                 445
Leu Val Ser Leu Asp Leu Pro Leu Asp Pro Leu Trp Glu Phe Pro Arg
    450                 455                 460
Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln
465                 470                 475                 480
Val Val Arg Ala Glu Ala Phe Gly Met Asp Pro Ala Arg Pro Asp Gln
                485                 490                 495
Ala Ser Thr Val Ala Val Lys Met Leu Lys Asp Asn Ala Ser Asp Lys
            500                 505                 510
Asp Leu Ala Asp Leu Val Ser Glu Met Glu Val Met Lys Leu Ile Gly
        515                 520                 525
Arg His Lys Asn Ile Ile Asn Leu Leu Gly Val Cys Thr Gln Glu Gly
    530                 535                 540
Pro Leu Tyr Val Ile Val Glu Cys Ala Ala Lys Gly Asn Leu Arg Glu
545                 550                 555                 560
Phe Leu Arg Ala Arg Arg Pro Pro Gly Pro Asp Leu Ser Pro Asp Gly
                565                 570                 575
Pro Arg Ser Ser Glu Gly Pro Leu Ser Phe Pro Val Leu Val Ser Cys
            580                 585                 590
Ala Tyr Gln Val Ala Arg Gly Met Gln Tyr Leu Glu Ser Arg Lys Cys
        595                 600                 605
Ile His Arg Asp Leu Ala Ala Xaa Asn Val Leu Val Thr Glu Asp Asn
    610                 615                 620
Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Gly Val His His Ile
625                 630                 635                 640
Asp Tyr Tyr Lys Lys Thr Ser Asn Gly Arg Leu Pro Val Lys Trp Met
                645                 650                 655
Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val
            660                 665                 670
Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly Ser
        675                 680                 685
Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Ser Leu Leu Arg Glu
    690                 695                 700
Gly His Arg Met Asp Arg Pro Pro His Cys Pro Pro Glu Leu Tyr Gly
705                 710                 715                 720
Leu Met Arg Glu Cys Trp His Ala Ala Pro Ser Gln Arg Pro Thr Phe
                725                 730                 735
Lys Gln Leu Val Glu Ala Leu Asp Lys Val Leu Leu Ala Val Ser Glu
            740                 745                 750
Glu Tyr Leu Asp Leu Arg Leu Thr Phe Gly Pro Tyr Ser Pro Ser Gly
        755                 760                 765
```

```
Gly Asp Ala Ser Ser Thr Cys Ser Ser Ser Asp Ser Val Phe Ser His
    770                 775                 780
Asp Pro Leu Pro Leu Gly Ser Ser Ser Phe Pro Phe Gly Ser Gly Val
785                 790                 795                 800
Gln Thr
```

<210> 304
<211> 993
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 835
<223> Xaa = D or Y or H or F

<220>
<221> VARIANT
<222> 836
<223> Xaa = I or S

<220>
<221> VARIANT
<222> 841
<223> Xaa = N or I

<220>
<221> VARIANT
<222> 842
<223> Xaa = Y or H

<400> 304

```
Met Pro Ala Leu Ala Arg Asp Ala Gly Thr Val Pro Leu Leu Val Val
 1               5                  10                  15
Phe Ser Ala Met Ile Phe Gly Thr Ile Thr Asn Gln Asp Leu Pro Val
            20                  25                  30
Ile Lys Cys Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly
        35                  40                  45
Lys Ser Ser Ser Tyr Pro Met Val Ser Glu Ser Pro Glu Asp Leu Gly
    50                  55                  60
Cys Ala Leu Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Ala
65                  70                  75                  80
Val Glu Val Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp
                85                  90                  95
Ala Pro Gly Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu
            100                 105                 110
Asn Cys Gln Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met
        115                 120                 125
Val Ile Leu Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe
    130                 135                 140
Ile Gln Ser Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile
145                 150                 155                 160
Arg Asn Thr Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met
                165                 170                 175
```

```
Glu Asn Gln Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro
            180                 185                 190
Ile Val Glu Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu
        195                 200                 205
Glu Ser Pro Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu
    210                 215                 220
Phe Gly Thr Asp Ile Arg Cys Cys Ala Arg Asn Glu Leu Gly Arg Glu
225                 230                 235                 240
Cys Thr Arg Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr
                245                 250                 255
Leu Pro Gln Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys
            260                 265                 270
Lys Ala Val His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu
        275                 280                 285
Asn Lys Ala Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser
    290                 295                 300
Thr Asn Arg Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val
305                 310                 315                 320
Ala Arg Asn Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro
                325                 330                 335
Ser Gln Ser Ala Leu Val Thr Ile Val Gly Lys Gly Phe Ile Asn Ala
            340                 345                 350
Thr Asn Ser Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys
        355                 360                 365
Phe Ser Val Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr
    370                 375                 380
Phe Ser Arg Lys Ser Phe Pro Cys Glu Gln Lys Gly Leu Asp Asn Gly
385                 390                 395                 400
Tyr Ser Ile Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr
                405                 410                 415
Ile Phe His Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr
            420                 425                 430
Leu Asn Ile Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser
        435                 440                 445
Gln Ala Ser Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp
    450                 455                 460
Lys Lys Cys Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu
465                 470                 475                 480
Gly Val Trp Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val
                485                 490                 495
Ser Ser Ser Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val
            500                 505                 510
Lys Cys Cys Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu
        515                 520                 525
Leu Asn Ser Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Ile Ser Phe
    530                 535                 540
Tyr Ala Thr Ile Gly Val Cys Leu Leu Phe Ile Val Val Leu Thr Leu
545                 550                 555                 560
Leu Ile Cys His Lys Tyr Lys Lys Gln Phe Arg Tyr Glu Ser Gln Leu
                565                 570                 575
Gln Met Val Gln Val Thr Gly Ser Ser Asp Asn Glu Tyr Phe Tyr Val
            580                 585                 590
Asp Phe Arg Glu Tyr Glu Tyr Asp Leu Lys Trp Glu Phe Pro Arg Glu
        595                 600                 605
Asn Leu Glu Phe Gly Lys Val Leu Gly Ser Gly Ala Phe Gly Lys Val
    610                 615                 620
```

```
Met Asn Ala Thr Ala Tyr Gly Ile Ser Lys Thr Gly Val Ser Ile Gln
625                 630                 635                 640
Val Ala Val Lys Met Leu Lys Glu Lys Ala Asp Ser Ser Glu Arg Glu
                645                 650                 655
Ala Leu Met Ser Glu Leu Lys Met Met Thr Gln Leu Gly Ser His Glu
            660                 665                 670
Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Leu Ser Gly Pro Ile Tyr
        675                 680                 685
Leu Ile Phe Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Tyr Leu Arg
    690                 695                 700
Ser Lys Arg Glu Lys Phe His Arg Thr Trp Thr Glu Ile Phe Lys Glu
705                 710                 715                 720
His Asn Phe Ser Phe Tyr Pro Thr Phe Gln Ser His Pro Asn Ser Ser
                725                 730                 735
Met Pro Gly Ser Arg Glu Val Gln Ile His Pro Asp Ser Asp Gln Ile
            740                 745                 750
Ser Gly Leu His Gly Asn Ser Phe His Ser Glu Asp Glu Ile Glu Tyr
        755                 760                 765
Glu Asn Gln Lys Arg Leu Glu Glu Glu Glu Asp Leu Asn Val Leu Thr
    770                 775                 780
Phe Glu Asp Leu Leu Cys Phe Ala Tyr Gln Val Ala Lys Gly Met Glu
785                 790                 795                 800
Phe Leu Glu Phe Lys Ser Cys Val His Arg Asp Leu Ala Ala Arg Asn
                805                 810                 815
Val Leu Val Thr His Gly Lys Val Val Lys Ile Cys Asp Phe Gly Leu
            820                 825                 830
Ala Arg Xaa Xaa Met Ser Asp Ser Xaa Xaa Val Val Arg Gly Asn Ala
        835                 840                 845
Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Leu Phe Glu Gly Ile
    850                 855                 860
Tyr Thr Ile Lys Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu
865                 870                 875                 880
Ile Phe Ser Leu Gly Val Asn Pro Tyr Pro Gly Ile Pro Val Asp Ala
                885                 890                 895
Asn Phe Tyr Lys Leu Ile Gln Asn Gly Phe Lys Met Asp Gln Pro Phe
            900                 905                 910
Tyr Ala Thr Glu Glu Ile Tyr Ile Ile Met Gln Ser Cys Trp Ala Phe
        915                 920                 925
Asp Ser Arg Lys Arg Pro Ser Phe Pro Asn Leu Thr Ser Phe Leu Gly
    930                 935                 940
Cys Gln Leu Ala Asp Ala Glu Glu Ala Met Tyr Gln Asn Val Asp Gly
945                 950                 955                 960
Arg Val Ser Glu Cys Pro His Thr Tyr Gln Asn Arg Arg Pro Phe Ser
                965                 970                 975
Arg Glu Met Asp Leu Gly Leu Leu Ser Pro Gln Ala Gln Val Glu Asp
            980                 985                 990
Ser
```

<210> 305
<211> 976
<212> PRT
<213> Homo sapiens

<220>

<221> VARIANT
<222> 541
<223> Xaa = M or L or V

<220>
<221> VARIANT
<222> 557
<223> Xaa = W or R

<220>
<221> VARIANT
<222> 664
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 788, 136
<223> Xaa = C or R

<220>
<221> VARIANT
<222> 802
<223> Xaa = T or I

<220>
<221> VARIANT
<222> 816, 820
<223> Xaa = D or V or H or Y

<220>
<221> VARIANT
<222> 822
<223> Xaa = N or Y or K

<220>
<221> VARIANT
<222> 823
<223> Xaa = Y or D or C

<220>
<221> VARIANT
<222> 835
<223> Xaa = W or R

<220>
<221> VARIANT
<222> 869
<223> Xaa = P or S

<220>
<221> VARIANT
<222> 900
<223> Xaa = Y or F

<220>
<221> VARIANT

<222> 52
<223> Xaa = D or N

<220>
<221> VARIANT
<222> 178
<223> Xaa = A or T

<400> 305

```
Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
 1               5                  10                  15
Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly
            20                  25                  30
Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
        35                  40                  45
Arg Val Gly Xaa Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
    50                  55                  60
Lys Trp Thr Phe Glu Ile Leu Asp Glu Thr Asn Glu Asn Lys Gln Asn
65                  70                  75                  80
Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
                85                  90                  95
Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
            100                 105                 110
Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
        115                 120                 125
Asp Asn Asp Thr Leu Val Arg Xaa Pro Leu Thr Asp Pro Glu Val Thr
    130                 135                 140
Asn Tyr Ser Leu Lys Gly Cys Gln Gly Lys Pro Leu Pro Lys Asp Leu
145                 150                 155                 160
Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
                165                 170                 175
Arg Xaa Tyr His Arg Leu Cys Leu His Cys Ser Val Asp Gln Glu Gly
            180                 185                 190
Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
        195                 200                 205
Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg
    210                 215                 220
Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
225                 230                 235                 240
Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
                245                 250                 255
Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
            260                 265                 270
Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
        275                 280                 285
Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
    290                 295                 300
Leu Glu Val Val Asp Lys Gly Phe Ile Asn Ile Phe Pro Met Ile Asn
305                 310                 315                 320
Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
                325                 330                 335
Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
            340                 345                 350
Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
        355                 360                 365
Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
```

```
    370                 375                 380
Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385                 390                 395                 400
Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Lys Pro Glu Ile Leu
                405                 410                 415
Thr Tyr Asp Arg Leu Val Asn Gly Met Leu Gln Cys Val Ala Ala Gly
            420                 425                 430
Phe Pro Glu Pro Thr Ile Asp Trp Tyr Phe Cys Pro Gly Thr Glu Gln
        435                 440                 445
Arg Cys Ser Ala Ser Val Leu Pro Val Asp Val Gln Thr Leu Asn Ser
    450                 455                 460
Ser Gly Pro Pro Phe Gly Lys Leu Val Val Gln Ser Ser Ile Asp Ser
465                 470                 475                 480
Ser Ala Phe Lys His Asn Gly Thr Val Glu Cys Lys Ala Tyr Asn Asp
                485                 490                 495
Val Gly Lys Thr Ser Ala Tyr Phe Asn Phe Ala Phe Lys Gly Asn Asn
            500                 505                 510
Lys Glu Gln Ile His Pro His Thr Leu Phe Thr Pro Leu Leu Ile Gly
        515                 520                 525
Phe Val Ile Val Ala Gly Met Met Cys Ile Ile Val Xaa Ile Leu Thr
    530                 535                 540
Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln Xaa Lys Val Val
545                 550                 555                 560
Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp Pro Thr Gln Leu
                565                 570                 575
Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg Leu Ser Phe Gly
            580                 585                 590
Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
        595                 600                 605
Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val Ala Val Lys Met
    610                 615                 620
Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala Leu Met Ser Glu
625                 630                 635                 640
Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn Ile Val Asn Leu
                645                 650                 655
Leu Gly Ala Cys Thr Ile Gly Xaa Pro Thr Leu Val Ile Thr Glu Tyr
            660                 665                 670
Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Arg Asp Ser
        675                 680                 685
Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala Ala Leu Tyr Lys
    690                 695                 700
Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp Ser Thr Asn Glu
705                 710                 715                 720
Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val Pro Thr Lys Ala
                725                 730                 735
Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile Glu Arg Asp Val
            740                 745                 750
Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu Asp Leu Glu Asp
        755                 760                 765
Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met Ala Phe Leu Ala
    770                 775                 780
Ser Lys Asn Xaa Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu
785                 790                 795                 800
Xaa His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly Leu Ala Arg Xaa
                805                 810                 815
Ile Lys Asn Xaa Ser Xaa Xaa Val Val Lys Gly Asn Ala Arg Leu Pro
```

```
            820                 825                 830
Val Lys Xaa Met Ala Pro Glu Ser Ile Phe Asn Cys Val Tyr Thr Phe
        835                 840                 845
Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp Glu Leu Phe Ser
    850                 855                 860
Leu Gly Ser Ser Xaa Tyr Pro Gly Met Pro Val Asp Ser Lys Phe Tyr
865                 870                 875                 880
Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro Glu His Ala Pro
                885                 890                 895
Ala Glu Met Xaa Asp Ile Met Lys Thr Cys Trp Asp Ala Asp Pro Leu
            900                 905                 910
Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile Glu Lys Gln Ile
        915                 920                 925
Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala Asn Cys Ser Pro
    930                 935                 940
Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg Ile Asn Ser Val
945                 950                 955                 960
Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val His Asp Asp Val
                965                 970                 975
```

<210> 306
<211> 1390
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 37, 145, 158, 237
<223> Xaa = V or A

<220>
<221> VARIANT
<222> 39, 1250
<223> Xaa = M or T

<220>
<221> VARIANT
<222> 42
<223> Xaa = Q or R

<220>
<221> VARIANT
<222> 113, 508
<223> Xaa = K or R

<220>
<221> VARIANT
<222> 114, 382
<223> Xaa = D or N

<220>
<221> VARIANT
<222> 148, 476, 1094
<223> Xaa = H or R

<220>
<221> VARIANT
<222> 151
<223> Xaa = T or P

<220>
<221> VARIANT
<222> 168
<223> Xaa = E or D

<220>
<221> VARIANT
<222> 193
<223> Xaa = I or T

<220>
<221> VARIANT
<222> 216
<223> Xaa = V or L

<220>
<221> VARIANT
<222> 276, 511, 729
<223> Xaa = T or A

<220>
<221> VARIANT
<222> 314
<223> Xaa = F or L

<220>
<221> VARIANT
<222> 337
<223> Xaa = L or P

<220>
<221> VARIANT
<222> 340
<223> Xaa = D or V

<220>
<221> VARIANT
<222> 400
<223> Xaa = R or G

<220>
<221> VARIANT
<222> 481
<223> Xaa = L or M

<220>
<221> VARIANT
<222> 500
<223> Xaa = D or G

<220>

<221> VARIANT
<222> 501, 542
<223> Xaa = Y or H

<220>
<221> VARIANT
<222> 622
<223> Xaa = L or S

<220>
<221> VARIANT
<222> 720
<223> Xaa = F or S

<220>
<221> VARIANT
<222> 1100
<223> Xaa = N or Y

<220>
<221> VARIANT
<222> 1230
<223> Xaa = C or Y

<220>
<221> VARIANT
<222> 1235
<223> Xaa = Y or D

<400> 306

```
Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
 1               5                  10                  15
Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
            20                  25                  30
Ser Glu Met Asn Xaa Asn Xaa Lys Tyr Xaa Leu Pro Asn Phe Thr Ala
        35                  40                  45
Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
    50                  55                  60
Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65                  70                  75                  80
Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
                85                  90                  95
Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
            100                 105                 110
Xaa Xaa Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
        115                 120                 125
Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
    130                 135                 140
Xaa Phe Pro Xaa Asn His Xaa Ala Asp Ile Gln Ser Glu Xaa His Cys
145                 150                 155                 160
Ile Phe Ser Pro Gln Ile Glu Xaa Pro Ser Gln Cys Pro Asp Cys Val
                165                 170                 175
Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
            180                 185                 190
Xaa Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
        195                 200                 205
```

```
His Pro Leu His Ser Ile Ser Xaa Arg Arg Leu Lys Glu Thr Lys Asp
    210                 215                 220
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Xaa Leu Pro Glu
225                 230                 235                 240
Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255
Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270
Thr Phe His Xaa Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285
His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300
Lys Lys Arg Ser Thr Lys Lys Glu Val Xaa Asn Ile Leu Gln Ala Ala
305                 310                 315                 320
Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335
Xaa Asn Asp Xaa Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350
Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365
Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Xaa Val Arg
    370                 375                 380
Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Xaa
385                 390                 395                 400
Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415
Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430
Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445
Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460
Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro Xaa Val Asn Phe Leu
465                 470                 475                 480
Xaa Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
Asn Gln Asn Xaa Xaa Thr Leu Val Ile Thr Gly Xaa Lys Ile Xaa Lys
            500                 505                 510
Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525
Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys Xaa Asp Lys
    530                 535                 540
Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560
Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575
Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590
Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605
Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Xaa Lys Cys
    610                 615                 620
Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640
Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655
```

```
Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670
Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685
His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700
Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Xaa
705                 710                 715                 720
Ala Val Lys Leu Lys Ile Asp Leu Xaa Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735
Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750
Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780
Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800
Cys Xaa Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815
Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830
Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845
Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
    850                 855                 860
Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865                 870                 875                 880
Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
                885                 890                 895
Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys
            900                 905                 910
Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp
        915                 920                 925
Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
    930                 935                 940
Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln
945                 950                 955                 960
Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His
                965                 970                 975
Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
            980                 985                 990
Thr Glu Met Val Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro
        995                 1000                1005
Glu Asp Gln Phe Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln Val
    1010                1015                1020
Gln Tyr Pro Leu Thr Asp Met Ser Pro Ile Leu Thr Ser Gly Asp Ser
1025                1030                1035                1040
Asp Ile Ser Ser Pro Leu Leu Gln Asn Thr Val His Ile Asp Leu Ser
                1045                1050                1055
Ala Leu Asn Pro Glu Leu Val Gln Ala Val Gln His Val Val Ile Gly
            1060                1065                1070
Pro Ser Ser Leu Ile Val His Phe Asn Glu Val Ile Gly Arg Gly His
        1075                1080                1085
Phe Gly Cys Val Tyr Xaa Gly Thr Leu Leu Asp Xaa Asp Gly Lys Lys
    1090                1095                1100
```

```
Ile His Cys Ala Val Lys Ser Leu Asn Arg Ile Thr Asp Ile Gly Glu
1105                1110                1115                1120
Val Ser Gln Phe Leu Thr Glu Gly Ile Ile Met Lys Asp Phe Ser His
                1125                1130                1135
Pro Asn Val Leu Ser Leu Leu Gly Ile Cys Leu Arg Ser Glu Gly Ser
            1140                1145                1150
Pro Leu Val Val Leu Pro Tyr Met Lys His Gly Asp Leu Arg Asn Phe
        1155                1160                1165
Ile Arg Asn Glu Thr His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe
    1170                1175                1180
Gly Leu Gln Val Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe
1185                1190                1195                1200
Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe
                1205                1210                1215
Thr Val Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Met Xaa Asp Lys
            1220                1225                1230
Glu Tyr Xaa Ser Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys
        1235                1240                1245
Trp Xaa Ala Leu Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys Ser
    1250                1255                1260
Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Leu Met Thr Arg Gly
1265                1270                1275                1280
Ala Pro Pro Tyr Pro Asp Val Asn Thr Phe Asp Ile Thr Val Tyr Leu
                1285                1290                1295
Leu Gln Gly Arg Arg Leu Leu Gln Pro Glu Tyr Cys Pro Asp Pro Leu
            1300                1305                1310
Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg Pro
        1315                1320                1325
Ser Phe Ser Glu Leu Val Ser Arg Ile Ser Ala Ile Phe Ser Thr Phe
    1330                1335                1340
Ile Gly Glu His Tyr Val His Val Asn Ala Thr Tyr Val Asn Val Lys
1345                1350                1355                1360
Cys Val Ala Pro Tyr Pro Ser Leu Leu Ser Ser Glu Asp Asn Ala Asp
                1365                1370                1375
Asp Glu Val Asp Thr Arg Pro Ala Ser Phe Trp Glu Thr Ser
            1380                1385                1390
```

<210> 307
<211> 1106
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 29
<223> Xaa = I or F

<220>
<221> VARIANT
<222> 194
<223> Xaa = I or T

<220>
<221> VARIANT
<222> 345

<223> Xaa = P or S

<400> 307

```
Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
 1               5                  10                  15
Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Xaa Ser Gln Gly
            20                  25                  30
Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
        35                  40                  45
Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
    50                  55                  60
Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65                  70                  75                  80
Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
                85                  90                  95
Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
            100                 105                 110
Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly Phe Leu
        115                 120                 125
Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
    130                 135                 140
Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145                 150                 155                 160
His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
                165                 170                 175
Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
            180                 185                 190
Thr Xaa Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg
        195                 200                 205
Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
    210                 215                 220
Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225                 230                 235                 240
Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
                245                 250                 255
Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
            260                 265                 270
Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
        275                 280                 285
Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
    290                 295                 300
Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu Leu Gly
305                 310                 315                 320
Glu Val Gly Thr Leu Gln Phe Ala Glu Leu His Arg Ser Arg Thr Leu
                325                 330                 335
Gln Val Val Phe Glu Ala Tyr Pro Xaa Pro Thr Val Leu Trp Phe Lys
            340                 345                 350
Asp Asn Arg Thr Leu Gly Asp Ser Ser Ala Gly Glu Ile Ala Leu Ser
        355                 360                 365
Thr Arg Asn Val Ser Glu Thr Arg Tyr Val Ser Glu Leu Thr Leu Val
    370                 375                 380
Arg Val Lys Val Ala Glu Ala Gly His Tyr Thr Met Arg Ala Phe His
385                 390                 395                 400
Glu Asp Ala Glu Val Gln Leu Ser Phe Gln Leu Gln Ile Asn Val Pro
                405                 410                 415
Val Arg Val Leu Glu Leu Ser Glu Ser His Pro Asp Ser Gly Glu Gln
```

```
                420                 425                 430
Thr Val Arg Cys Arg Gly Arg Gly Met Pro Gln Pro Asn Ile Ile Trp
        435                 440                 445
Ser Ala Cys Arg Asp Leu Lys Arg Cys Pro Arg Glu Leu Pro Pro Thr
    450                 455                 460
Leu Leu Gly Asn Ser Ser Glu Glu Glu Ser Gln Leu Glu Thr Asn Val
465                 470                 475                 480
Thr Tyr Trp Glu Glu Glu Gln Glu Phe Glu Val Val Ser Thr Leu Arg
                485                 490                 495
Leu Gln His Val Asp Arg Pro Leu Ser Val Arg Cys Thr Leu Arg Asn
            500                 505                 510
Ala Val Gly Gln Asp Thr Gln Glu Val Ile Val Val Pro His Ser Leu
        515                 520                 525
Pro Phe Lys Val Val Val Ile Ser Ala Ile Leu Ala Leu Val Val Leu
    530                 535                 540
Thr Ile Ile Ser Leu Ile Ile Leu Ile Met Leu Trp Gln Lys Lys Pro
545                 550                 555                 560
Arg Tyr Glu Ile Arg Trp Lys Val Ile Glu Ser Val Ser Ser Asp Gly
                565                 570                 575
His Glu Tyr Ile Tyr Val Asp Pro Met Gln Leu Pro Tyr Asp Ser Thr
            580                 585                 590
Trp Glu Leu Pro Arg Asp Gln Leu Val Leu Gly Arg Thr Leu Gly Ser
        595                 600                 605
Gly Ala Phe Gly Gln Val Val Glu Ala Thr Ala His Gly Leu Ser His
    610                 615                 620
Ser Gln Ala Thr Met Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala
625                 630                 635                 640
Arg Ser Ser Glu Lys Gln Ala Leu Met Ser Glu Leu Lys Ile Met Ser
                645                 650                 655
His Leu Gly Pro His Leu Asn Val Val Asn Leu Leu Gly Ala Cys Thr
            660                 665                 670
Lys Gly Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Arg Tyr Gly Asp
        675                 680                 685
Leu Val Asp Tyr Leu His Arg Asn Lys His Thr Phe Leu Gln His His
    690                 695                 700
Ser Asp Lys Arg Arg Pro Pro Ser Ala Glu Leu Tyr Ser Asn Ala Leu
705                 710                 715                 720
Pro Val Gly Leu Pro Leu Pro Ser His Val Ser Leu Thr Gly Glu Ser
                725                 730                 735
Asp Gly Gly Tyr Met Asp Met Ser Lys Asp Glu Ser Val Asp Tyr Val
            740                 745                 750
Pro Met Leu Asp Met Lys Gly Asp Val Lys Tyr Ala Asp Ile Glu Ser
        755                 760                 765
Ser Asn Tyr Met Ala Pro Tyr Asp Asn Tyr Val Pro Ser Ala Pro Glu
    770                 775                 780
Arg Thr Cys Arg Ala Thr Leu Ile Asn Glu Ser Pro Val Leu Ser Tyr
785                 790                 795                 800
Met Asp Leu Val Gly Phe Ser Tyr Gln Val Ala Asn Gly Met Glu Phe
                805                 810                 815
Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn Val
            820                 825                 830
Leu Ile Cys Glu Gly Lys Leu Val Lys Ile Cys Asp Phe Gly Leu Ala
        835                 840                 845
Arg Asp Ile Met Arg Asp Ser Asn Tyr Ile Ser Lys Gly Ser Thr Phe
    850                 855                 860
Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Ser Leu Tyr
```

```
865                 870                 875                 880
Thr Thr Leu Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile
                885                 890                 895
Phe Thr Leu Gly Gly Thr Pro Tyr Pro Glu Leu Pro Met Asn Glu Gln
            900                 905                 910
Phe Tyr Asn Ala Ile Lys Arg Gly Tyr Arg Met Ala Gln Pro Ala His
        915                 920                 925
Ala Ser Asp Glu Ile Tyr Glu Ile Met Gln Lys Cys Trp Glu Glu Lys
    930                 935                 940
Phe Glu Ile Arg Pro Pro Phe Ser Gln Leu Val Leu Leu Leu Glu Arg
945                 950                 955                 960
Leu Leu Gly Glu Gly Tyr Lys Lys Lys Tyr Gln Gln Val Asp Glu Glu
                965                 970                 975
Phe Leu Arg Ser Asp His Pro Ala Ile Leu Arg Ser Gln Ala Arg Leu
            980                 985                 990
Pro Gly Phe His Gly Leu Arg Ser Pro Leu Asp Thr Ser Ser Val Leu
        995                 1000                1005
Tyr Thr Ala Val Gln Pro Asn Glu Gly Asp Asn Asp Tyr Ile Ile Pro
    1010                1015                1020
Leu Pro Asp Pro Lys Pro Glu Val Ala Asp Glu Gly Pro Leu Glu Gly
1025                1030                1035                1040
Ser Pro Ser Leu Ala Ser Ser Thr Leu Asn Glu Val Asn Thr Ser Ser
                1045                1050                1055
Thr Ile Ser Cys Asp Ser Pro Leu Glu Pro Gln Asp Glu Pro Glu Pro
            1060                1065                1070
Glu Pro Gln Leu Glu Leu Gln Val Glu Pro Glu Pro Glu Leu Glu Gln
        1075                1080                1085
Leu Pro Asp Ser Gly Cys Pro Ala Pro Arg Ala Glu Ala Glu Asp Ser
    1090                1095                1100
Phe Leu
1105


<210> 308
<211> 1400
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 113, 1195
<223> Xaa = G or S

<220>
<221> VARIANT
<222> 209
<223> Xaa = G or A

<220>
<221> VARIANT
<222> 322, 523
<223> Xaa = Q or R

<220>
<221> VARIANT
<222> 440
```

<223> Xaa = N or S

<220>
<221> VARIANT
<222> 946
<223> Xaa = V or M

<220>
<221> VARIANT
<222> 1232
<223> Xaa = R or G or D or V

<220>
<221> VARIANT
<222> 1254
<223> Xaa = M or T

<220>
<221> VARIANT
<222> 1335
<223> Xaa = R or G

<400> 308

```
Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
 1               5                  10                  15
Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20                  25                  30
Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35                  40                  45
Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50                  55                  60
Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65                  70                  75                  80
Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85                  90                  95
Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100                 105                 110
Xaa Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115                 120                 125
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140
Leu His Asp Leu Glu Pro Gln Gly Thr Ala Val His Leu Ala Ala Pro
145                 150                 155                 160
Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175
Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190
Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205
Xaa Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220
Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240
His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255
Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
```

```
            260                 265                 270
Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285
Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300
Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320
Leu Xaa Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335
Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350
Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365
Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380
Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415
Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
            420                 425                 430
Phe Ser Arg Val Asp Leu Phe Xaa Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445
Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460
Gly Thr Met Asp Gly Arg Ile Leu Gln Val Glu Leu Val Arg Ser Leu
465                 470                 475                 480
Asn Tyr Leu Leu Tyr Val Ser Asn Phe Ser Leu Gly Asp Ser Gly Gln
                485                 490                 495
Pro Val Gln Arg Asp Val Ser Arg Leu Gly Asp His Leu Leu Phe Ala
            500                 505                 510
Ser Gly Asp Gln Val Phe Gln Val Pro Ile Xaa Gly Pro Gly Cys Arg
        515                 520                 525
His Phe Leu Thr Cys Gly Arg Cys Leu Arg Ala Trp His Phe Met Gly
    530                 535                 540
Cys Gly Trp Cys Gly Asn Met Cys Gly Gln Gln Lys Glu Cys Pro Gly
545                 550                 555                 560
Ser Trp Gln Gln Asp His Cys Pro Pro Lys Leu Thr Glu Phe His Pro
                565                 570                 575
His Ser Gly Pro Leu Arg Gly Ser Thr Arg Leu Thr Leu Cys Gly Ser
            580                 585                 590
Asn Phe Tyr Leu His Pro Ser Gly Leu Val Pro Glu Gly Thr His Gln
        595                 600                 605
Val Thr Val Gly Gln Ser Pro Cys Arg Pro Leu Pro Lys Asp Ser Ser
    610                 615                 620
Lys Leu Arg Pro Val Pro Arg Lys Asp Phe Val Glu Glu Phe Glu Cys
625                 630                 635                 640
Glu Leu Glu Pro Leu Gly Thr Gln Ala Val Gly Pro Thr Asn Val Ser
                645                 650                 655
Leu Thr Val Thr Asn Met Pro Pro Gly Lys His Phe Arg Val Asp Gly
            660                 665                 670
Thr Ser Val Leu Arg Gly Phe Ser Phe Met Glu Pro Val Leu Ile Ala
        675                 680                 685
Val Gln Pro Leu Phe Gly Pro Arg Ala Gly Gly Thr Cys Leu Thr Leu
    690                 695                 700
Glu Gly Gln Ser Leu Ser Val Gly Thr Ser Arg Ala Val Leu Val Asn
```

705 710 715 720
Gly Thr Glu Cys Leu Leu Ala Arg Val Ser Glu Gly Gln Leu Leu Cys
725 730 735
Ala Thr Pro Pro Gly Ala Thr Val Ala Ser Val Pro Leu Ser Leu Gln
740 745 750
Val Gly Gly Ala Gln Val Pro Gly Ser Trp Thr Phe Gln Tyr Arg Glu
755 760 765
Asp Pro Val Val Leu Ser Ile Ser Pro Asn Cys Gly Tyr Ile Asn Ser
770 775 780
His Ile Thr Ile Cys Gly Gln His Leu Thr Ser Ala Trp His Leu Val
785 790 795 800
Leu Ser Phe His Asp Gly Leu Arg Ala Val Glu Ser Arg Cys Glu Arg
805 810 815
Gln Leu Pro Glu Gln Gln Leu Cys Arg Leu Pro Glu Tyr Val Val Arg
820 825 830
Asp Pro Gln Gly Trp Val Ala Gly Asn Leu Ser Ala Arg Gly Asp Gly
835 840 845
Ala Ala Gly Phe Thr Leu Pro Gly Phe Arg Phe Leu Pro Pro Pro His
850 855 860
Pro Pro Ser Ala Asn Leu Val Pro Leu Lys Pro Glu Glu His Ala Ile
865 870 875 880
Lys Phe Glu Tyr Ile Gly Leu Gly Ala Val Ala Asp Cys Val Gly Ile
885 890 895
Asn Val Thr Val Gly Gly Glu Ser Cys Gln His Glu Phe Arg Gly Asp
900 905 910
Met Val Val Cys Pro Leu Pro Pro Ser Leu Gln Leu Gly Gln Asp Gly
915 920 925
Ala Pro Leu Gln Val Cys Val Asp Gly Glu Cys His Ile Leu Gly Arg
930 935 940
Val Xaa Arg Pro Gly Pro Asp Gly Val Pro Gln Ser Thr Leu Leu Gly
945 950 955 960
Ile Leu Leu Pro Leu Leu Leu Leu Val Ala Ala Leu Ala Thr Ala Leu
965 970 975
Val Phe Ser Tyr Trp Trp Arg Arg Lys Gln Leu Val Leu Pro Pro Asn
980 985 990
Leu Asn Asp Leu Ala Ser Leu Asp Gln Thr Ala Gly Ala Thr Pro Leu
995 1000 1005
Pro Ile Leu Tyr Ser Gly Ser Asp Tyr Arg Ser Gly Leu Ala Leu Pro
1010 1015 1020
Ala Ile Asp Gly Leu Asp Ser Thr Thr Cys Val His Gly Ala Ser Phe
1025 1030 1035 1040
Ser Asp Ser Glu Asp Glu Ser Cys Val Pro Leu Leu Arg Lys Glu Ser
1045 1050 1055
Ile Gln Leu Arg Asp Leu Asp Ser Ala Leu Leu Ala Glu Val Lys Asp
1060 1065 1070
Val Leu Ile Pro His Glu Arg Val Val Thr His Ser Asp Arg Val Ile
1075 1080 1085
Gly Lys Gly His Phe Gly Val Val Tyr His Gly Glu Tyr Ile Asp Gln
1090 1095 1100
Ala Gln Asn Arg Ile Gln Cys Ala Ile Lys Ser Leu Ser Arg Ile Thr
1105 1110 1115 1120
Glu Met Gln Gln Val Glu Ala Phe Leu Arg Glu Gly Leu Leu Met Arg
1125 1130 1135
Gly Leu Asn His Pro Asn Val Leu Ala Leu Ile Gly Ile Met Leu Pro
1140 1145 1150
Pro Glu Gly Leu Pro His Val Leu Leu Pro Tyr Met Cys His Gly Asp

```
        1155                1160                1165
Leu Leu Gln Phe Ile Arg Ser Pro Gln Arg Asn Pro Thr Val Lys Asp
    1170                1175                1180
Leu Ile Ser Phe Gly Leu Gln Val Ala Arg Xaa Met Glu Tyr Leu Ala
1185                1190                1195                1200
Glu Gln Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu
                1205                1210                1215
Asp Glu Ser Phe Thr Val Lys Val Ala Asp Phe Gly Leu Ala Arg Xaa
            1220                1225                1230
Ile Leu Asp Arg Glu Tyr Tyr Ser Val Gln Gln His Arg His Ala Arg
        1235                1240                1245
Leu Pro Val Lys Trp Xaa Ala Leu Glu Ser Leu Gln Thr Tyr Arg Phe
    1250                1255                1260
Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Leu
1265                1270                1275                1280
Leu Thr Arg Gly Ala Pro Pro Tyr Arg His Ile Asp Pro Phe Asp Leu
                1285                1290                1295
Thr His Phe Leu Ala Gln Gly Arg Arg Leu Pro Gln Pro Glu Tyr Cys
            1300                1305                1310
Pro Asp Ser Leu Tyr Gln Val Met Gln Gln Cys Trp Glu Ala Asp Pro
        1315                1320                1325
Ala Val Arg Pro Thr Phe Xaa Val Leu Val Gly Glu Val Glu Gln Ile
    1330                1335                1340
Val Ser Ala Leu Leu Gly Asp His Tyr Val Gln Leu Pro Ala Thr Tyr
1345                1350                1355                1360
Met Asn Leu Gly Pro Ser Thr Ser His Glu Met Asn Val Arg Pro Glu
                1365                1370                1375
Gln Pro Gln Phe Ser Pro Met Pro Gly Asn Val Arg Arg Pro Arg Pro
            1380                1385                1390
Leu Ser Glu Pro Pro Arg Pro Thr
        1395                1400
```

<210> 309
<211> 1124
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 346
<223> Xaa = P or Q

<220>
<221> VARIANT
<222> 486
<223> Xaa = V or I

<220>
<221> VARIANT
<222> 695
<223> Xaa = I or T

<220>
<221> VARIANT
<222> 724

<223> Xaa = A or T

<220>
<221> VARIANT
<222> 849
<223> Xaa = R or W

<400> 309

```
Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1               5                  10                  15
Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30
Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45
Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60
Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95
Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110
Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125
Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140
Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160
Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175
His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190
Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205
Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220
Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240
Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255
Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270
Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285
Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
    290                 295                 300
Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305                 310                 315                 320
Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
                325                 330                 335
Gly Leu Gln Cys Glu Arg Glu Gly Ile Xaa Arg Met Thr Pro Lys Ile
            340                 345                 350
Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
        355                 360                 365
Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
    370                 375                 380
```

```
Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
385                 390                 395                 400
Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
                405                 410                 415
Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
            420                 425                 430
Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
        435                 440                 445
Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
    450                 455                 460
Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
465                 470                 475                 480
Leu Leu Tyr Lys Pro Xaa Asn His Tyr Glu Ala Trp Gln His Ile Gln
                485                 490                 495
Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
            500                 505                 510
Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly
        515                 520                 525
His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro
    530                 535                 540
Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn
545                 550                 555                 560
Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val
                565                 570                 575
Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys
            580                 585                 590
Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg
        595                 600                 605
Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu
    610                 615                 620
Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro
625                 630                 635                 640
Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val
                645                 650                 655
Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile
            660                 665                 670
Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys
        675                 680                 685
Ile Lys Asn Ala Thr Ile Xaa Gln Tyr Gln Leu Lys Gly Leu Glu Pro
    690                 695                 700
Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser
705                 710                 715                 720
Ser Asn Pro Xaa Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln
                725                 730                 735
Ala Pro Ala Asp Leu Gly Gly Gly Lys Met Leu Leu Ile Ala Ile Leu
            740                 745                 750
Gly Ser Ala Gly Met Thr Cys Leu Thr Val Leu Leu Ala Phe Leu Ile
        755                 760                 765
Ile Leu Gln Leu Lys Arg Ala Asn Val Gln Arg Arg Met Ala Gln Ala
    770                 775                 780
Phe Gln Asn Val Arg Glu Glu Pro Ala Val Gln Phe Asn Ser Gly Thr
785                 790                 795                 800
Leu Ala Leu Asn Arg Lys Val Lys Asn Asn Pro Asp Pro Thr Ile Tyr
                805                 810                 815
Pro Val Leu Asp Trp Asn Asp Ile Lys Phe Gln Asp Val Ile Gly Glu
            820                 825                 830
```

```
Gly Asn Phe Gly Gln Val Leu Lys Ala Arg Ile Lys Lys Asp Gly Leu
        835                 840                 845
Xaa Met Asp Ala Ala Ile Lys Arg Met Lys Glu Tyr Ala Ser Lys Asp
    850                 855                 860
Asp His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly
865                 870                 875                 880
His His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Glu His Arg Gly
                885                 890                 895
Tyr Leu Tyr Leu Ala Ile Glu Tyr Ala Pro His Gly Asn Leu Leu Asp
            900                 905                 910
Phe Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Ile
        915                 920                 925
Ala Asn Ser Thr Ala Ser Thr Leu Ser Ser Gln Gln Leu Leu His Phe
    930                 935                 940
Ala Ala Asp Val Ala Arg Gly Met Asp Tyr Leu Ser Gln Lys Gln Phe
945                 950                 955                 960
Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Gly Glu Asn Tyr
                965                 970                 975
Val Ala Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Gln Glu Val Tyr
            980                 985                 990
Val Lys Lys Thr Met Gly Arg Leu Pro Val Arg Trp Met Ala Ile Glu
        995                 1000                1005
Ser Leu Asn Tyr Ser Val Tyr Thr Thr Asn Ser Asp Val Trp Ser Tyr
    1010                1015                1020
Gly Val Leu Leu Trp Glu Ile Val Ser Leu Gly Gly Thr Pro Tyr Cys
1025                1030                1035                1040
Gly Met Thr Cys Ala Glu Leu Tyr Glu Lys Leu Pro Gln Gly Tyr Arg
                1045                1050                1055
Leu Glu Lys Pro Leu Asn Cys Asp Asp Glu Val Tyr Asp Leu Met Arg
            1060                1065                1070
Gln Cys Trp Arg Glu Lys Pro Tyr Glu Arg Pro Ser Phe Ala Gln Ile
        1075                1080                1085
Leu Val Ser Leu Asn Arg Met Leu Glu Glu Arg Lys Thr Tyr Val Asn
    1090                1095                1100
Thr Thr Leu Tyr Glu Lys Phe Thr Tyr Ala Gly Ile Asp Cys Ser Ala
1105                1110                1115                1120
Glu Glu Ala Ala
```

<210> 310
<211> 1138
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 142
<223> Xaa = A or T

<220>
<221> VARIANT
<222> 1109
<223> Xaa = R or C

<400> 310

```
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
 1               5                  10                  15
Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30
Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45
Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60
Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80
Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95
Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110
Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125
Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Xaa Val Leu
    130                 135                 140
Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160
Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175
Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190
Tyr Ser Ala Thr Tyr Leu Glu Ala Ser Pro Leu Gly Ser Ala Phe Phe
        195                 200                 205
Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220
Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240
Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
                245                 250                 255
Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285
Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300
Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305                 310                 315                 320
Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
                325                 330                 335
Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp Arg Ile Pro Gln
            340                 345                 350
Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu Glu Thr Met Pro
        355                 360                 365
Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser
    370                 375                 380
Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Ser Thr Lys Ala
385                 390                 395                 400
Ile Val Glu Pro Glu Lys Thr Thr Ala Glu Phe Glu Val Pro Arg Leu
                405                 410                 415
Val Leu Ala Asp Ser Gly Phe Trp Glu Cys Arg Val Ser Thr Ser Gly
            420                 425                 430
Gly Gln Asp Ser Arg Arg Phe Lys Val Asn Val Lys Val Pro Pro Val
        435                 440                 445
```

```
Pro Leu Ala Ala Pro Arg Leu Leu Thr Lys Gln Ser Arg Gln Leu Val
    450                 455                 460
Val Ser Pro Leu Val Ser Phe Ser Gly Asp Gly Pro Ile Ser Thr Val
465                 470                 475                 480
Arg Leu His Tyr Arg Pro Gln Asp Ser Thr Met Asp Trp Ser Thr Ile
                485                 490                 495
Val Val Asp Pro Ser Glu Asn Val Thr Leu Met Asn Leu Arg Pro Lys
            500                 505                 510
Thr Gly Tyr Ser Val Arg Val Gln Leu Ser Arg Pro Gly Glu Gly Gly
        515                 520                 525
Glu Gly Ala Trp Gly Pro Pro Thr Leu Met Thr Thr Asp Cys Pro Glu
    530                 535                 540
Pro Leu Leu Gln Pro Trp Leu Glu Gly Trp His Val Glu Gly Thr Asp
545                 550                 555                 560
Arg Leu Arg Val Ser Trp Ser Leu Pro Leu Val Pro Gly Pro Leu Val
                565                 570                 575
Gly Asp Gly Phe Leu Leu Arg Leu Trp Asp Gly Thr Arg Gly Gln Glu
            580                 585                 590
Arg Arg Glu Asn Val Ser Ser Pro Gln Ala Arg Thr Ala Leu Leu Thr
        595                 600                 605
Gly Leu Thr Pro Gly Thr His Tyr Gln Leu Asp Val Gln Leu Tyr His
    610                 615                 620
Cys Thr Leu Leu Gly Pro Ala Ser Pro Pro Ala His Val Leu Leu Pro
625                 630                 635                 640
Pro Ser Gly Pro Pro Ala Pro Arg His Leu His Ala Gln Ala Leu Ser
                645                 650                 655
Asp Ser Glu Ile Gln Leu Thr Trp Lys His Pro Glu Ala Leu Pro Gly
            660                 665                 670
Pro Ile Ser Lys Tyr Val Val Glu Val Gln Val Ala Gly Gly Ala Gly
        675                 680                 685
Asp Pro Leu Trp Ile Asp Val Asp Arg Pro Glu Glu Thr Ser Thr Ile
    690                 695                 700
Ile Arg Gly Leu Asn Ala Ser Thr Arg Tyr Leu Phe Arg Met Arg Ala
705                 710                 715                 720
Ser Ile Gln Gly Leu Gly Asp Trp Ser Asn Thr Val Glu Glu Ser Thr
                725                 730                 735
Leu Gly Asn Gly Leu Gln Ala Glu Gly Pro Val Gln Glu Ser Arg Ala
            740                 745                 750
Ala Glu Glu Gly Leu Asp Gln Gln Leu Ile Leu Ala Val Val Gly Ser
        755                 760                 765
Val Ser Ala Thr Cys Leu Thr Ile Leu Ala Ala Leu Leu Thr Leu Val
    770                 775                 780
Cys Ile Arg Arg Ser Cys Leu His Arg Arg Arg Thr Phe Thr Tyr Gln
785                 790                 795                 800
Ser Gly Ser Gly Glu Glu Thr Ile Leu Gln Phe Ser Ser Gly Thr Leu
                805                 810                 815
Thr Leu Thr Arg Arg Pro Lys Leu Gln Pro Glu Pro Leu Ser Tyr Pro
            820                 825                 830
Val Leu Glu Trp Glu Asp Ile Thr Phe Glu Asp Leu Ile Gly Glu Gly
        835                 840                 845
Asn Phe Gly Gln Val Ile Arg Ala Met Ile Lys Lys Asp Gly Leu Lys
    850                 855                 860
Met Asn Ala Ala Ile Lys Met Leu Lys Glu Tyr Ala Ser Glu Asn Asp
865                 870                 875                 880
His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly His
                885                 890                 895
```

```
His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Lys Asn Arg Gly Tyr
            900                 905                 910
Leu Tyr Ile Ala Ile Glu Tyr Ala Pro Tyr Gly Asn Leu Leu Asp Phe
        915                 920                 925
Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Arg Glu
    930                 935                 940
His Gly Thr Ala Ser Thr Leu Ser Ser Arg Gln Leu Leu Arg Phe Ala
945                 950                 955                 960
Ser Asp Ala Ala Asn Gly Met Gln Tyr Leu Ser Glu Lys Gln Phe Ile
                965                 970                 975
His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Gly Glu Asn Leu Ala
            980                 985                 990
Ser Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Glu Glu Val Tyr Val
        995                 1000                1005
Lys Lys Thr Met Gly Arg Leu Pro Val Arg Trp Met Ala Ile Glu Ser
    1010                1015                1020
Leu Asn Tyr Ser Val Tyr Thr Thr Lys Ser Asp Val Trp Ser Phe Gly
1025                1030                1035                1040
Val Leu Leu Trp Glu Ile Val Ser Leu Gly Gly Thr Pro Tyr Cys Gly
                1045                1050                1055
Met Thr Cys Ala Glu Leu Tyr Glu Lys Leu Pro Gln Gly Tyr Arg Met
            1060                1065                1070
Glu Gln Pro Arg Asn Cys Asp Asp Glu Val Tyr Glu Leu Met Arg Gln
        1075                1080                1085
Cys Trp Arg Asp Arg Pro Tyr Glu Arg Pro Pro Phe Ala Gln Ile Ala
    1090                1095                1100
Leu Gln Leu Gly Xaa Met Leu Glu Ala Arg Lys Ala Tyr Val Asn Met
1105                1110                1115                1120
Ser Leu Phe Glu Asn Phe Thr Tyr Ala Gly Ile Asp Ala Thr Ala Glu
                1125                1130                1135
Glu Ala


<210> 311
<211> 455
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 75
<223> Xaa = P or I

<220>
<221> VARIANT
<222> 121
<223> Xaa = R or Q

<220>
<221> VARIANT
<222> 305
<223> Xaa = P or T

<400> 311
Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu
```

```
 1               5                  10                  15
Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro
            20                  25                  30
His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys
        35                  40                  45
Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys
    50                  55                  60
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Xaa Gly Gln Asp Thr Asp
65                  70                  75                  80
Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu
                85                  90                  95
Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val
            100                 105                 110
Glu Ile Ser Ser Cys Thr Val Asp Xaa Asp Thr Val Cys Gly Cys Arg
        115                 120                 125
Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe
    130                 135                 140
Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
145                 150                 155                 160
Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu
                165                 170                 175
Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr
            180                 185                 190
Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser
        195                 200                 205
Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu
    210                 215                 220
Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
225                 230                 235                 240
Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu
                245                 250                 255
Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser
            260                 265                 270
Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val
        275                 280                 285
Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys
    290                 295                 300
Xaa Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
305                 310                 315                 320
Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn
                325                 330                 335
Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp
            340                 345                 350
Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro
        355                 360                 365
Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu
    370                 375                 380
Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
385                 390                 395                 400
Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala
                405                 410                 415
Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly
            420                 425                 430
Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro
        435                 440                 445
Pro Ala Pro Ser Leu Leu Arg
```

450 455

<210> 312
<211> 461
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 187
<223> Xaa = V or M

<220>
<221> VARIANT
<222> 196
<223> Xaa = M or R

<220>
<221> VARIANT
<222> 232
<223> Xaa = E or K

<220>
<221> VARIANT
<222> 236
<223> Xaa = A or T

<220>
<221> VARIANT
<222> 264
<223> Xaa = L or P

<220>
<221> VARIANT
<222> 295
<223> Xaa = Q or R

<400> 312
Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15
Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
20 25 30
Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
35 40 45
Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
50 55 60
Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65 70 75 80
Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
85 90 95
Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
100 105 110
Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
115 120 125
Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg

```
    130                 135                 140
Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
145                 150                 155                 160
Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
                165                 170                 175
Asp Ile Cys Arg Pro His Gln Ile Cys Asn Xaa Val Ala Ile Pro Gly
            180                 185                 190
Asn Ala Ser Xaa Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
        195                 200                 205
Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210                 215                 220
Gln His Thr Gln Pro Thr Pro Xaa Pro Ser Thr Xaa Pro Ser Thr Ser
225                 230                 235                 240
Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
                245                 250                 255
Asp Phe Ala Leu Pro Val Gly Xaa Ile Val Gly Val Thr Ala Leu Gly
            260                 265                 270
Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
        275                 280                 285
Lys Lys Pro Leu Cys Leu Xaa Arg Glu Ala Lys Val Pro His Leu Pro
    290                 295                 300
Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305                 310                 315                 320
Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
                325                 330                 335
Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
            340                 345                 350
Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
        355                 360                 365
Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
    370                 375                 380
Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385                 390                 395                 400
Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
                405                 410                 415
Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
            420                 425                 430
Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
        435                 440                 445
Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
    450                 455                 460
```

<210> 313
<211> 1356
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 297, 952
<223> Xaa = V or I

<220>
<221> VARIANT
<222> 349

<223> Xaa = R or K

<220>
<221> VARIANT
<222> 392
<223> Xaa = D or N

<220>
<221> VARIANT
<222> 472
<223> Xaa = Q or H

<220>
<221> VARIANT
<222> 772
<223> Xaa = A or T

<220>
<221> VARIANT
<222> 787
<223> Xaa = R or G

<220>
<221> VARIANT
<222> 835
<223> Xaa = K or N

<220>
<221> VARIANT
<222> 848
<223> Xaa = V or E

<220>
<221> VARIANT
<222> 1147
<223> Xaa = P or S

<220>
<221> VARIANT
<222> 1210
<223> Xaa = P or A

<220>
<221> VARIANT
<222> 1347
<223> Xaa = S or T

<400> 313

```
Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
 1               5                  10                  15
Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
            20                  25                  30
Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
        35                  40                  45
Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
    50                  55                  60
```

```
Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65                  70                  75                  80
Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
                85                  90                  95
Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
            100                 105                 110
Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
        115                 120                 125
Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
    130                 135                 140
Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145                 150                 155                 160
Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                165                 170                 175
Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
            180                 185                 190
Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
        195                 200                 205
Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220
Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225                 230                 235                 240
Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255
Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270
Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285
Leu Ser Thr Leu Thr Ile Asp Gly Xaa Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300
Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320
Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335
Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Xaa Ile Pro Ala
            340                 345                 350
Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365
Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
    370                 375                 380
Ile Met Glu Val Ser Glu Arg Xaa Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400
Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415
Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430
Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445
Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460
Glu Cys Ala Asn Glu Pro Ser Xaa Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480
Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495
Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510
```

```
Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525
Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540
Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560
Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575
Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590
Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
        595                 600                 605
Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
    610                 615                 620
Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625                 630                 635                 640
Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
                645                 650                 655
Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
            660                 665                 670
Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
        675                 680                 685
Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
    690                 695                 700
Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705                 710                 715                 720
Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
                725                 730                 735
Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
            740                 745                 750
Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
        755                 760                 765
Val Gly Thr Xaa Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
    770                 775                 780
Ile Leu Xaa Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785                 790                 795                 800
Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
                805                 810                 815
Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp
            820                 825                 830
Arg Leu Xaa Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Xaa
        835                 840                 845
Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
    850                 855                 860
Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865                 870                 875                 880
Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
                885                 890                 895
Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
            900                 905                 910
Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
        915                 920                 925
Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
    930                 935                 940
Phe Arg Gln Gly Lys Asp Tyr Xaa Gly Ala Ile Pro Val Asp Leu Lys
945                 950                 955                 960
```

```
Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
                965                 970                 975
Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
            980                 985                 990
Glu Asp Leu Tyr Lys Asp Phe Leu Thr Leu Glu His Leu Ile Cys Tyr
        995                 1000                1005
Ser Phe Gln Val Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys
    1010                1015                1020
Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn
1025                1030                1035                1040
Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp
                1045                1050                1055
Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met
            1060                1065                1070
Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val
        1075                1080                1085
Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser
    1090                1095                1100
Pro Tyr Pro Gly Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys
1105                1110                1115                1120
Glu Gly Thr Arg Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr
                1125                1130                1135
Gln Thr Met Leu Asp Cys Trp His Gly Glu Xaa Ser Gln Arg Pro Thr
            1140                1145                1150
Phe Ser Glu Leu Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala
        1155                1160                1165
Gln Gln Asp Gly Lys Asp Tyr Ile Val Leu Pro Ile Ser Glu Thr Leu
    1170                1175                1180
Ser Met Glu Glu Asp Ser Gly Leu Ser Leu Pro Thr Ser Pro Val Ser
1185                1190                1195                1200
Cys Met Glu Glu Glu Glu Val Cys Asp Xaa Lys Phe His Tyr Asp Asn
                1205                1210                1215
Thr Ala Gly Ile Ser Gln Tyr Leu Gln Asn Ser Lys Arg Lys Ser Arg
            1220                1225                1230
Pro Val Ser Val Lys Thr Phe Glu Asp Ile Pro Leu Glu Glu Pro Glu
        1235                1240                1245
Val Lys Val Ile Pro Asp Asp Asn Gln Thr Asp Ser Gly Met Val Leu
    1250                1255                1260
Ala Ser Glu Glu Leu Lys Thr Leu Glu Asp Arg Thr Lys Leu Ser Pro
1265                1270                1275                1280
Ser Phe Gly Gly Met Val Pro Ser Lys Ser Arg Glu Ser Val Ala Ser
                1285                1290                1295
Glu Gly Ser Asn Gln Thr Ser Gly Tyr Gln Ser Gly Tyr His Ser Asp
            1300                1305                1310
Asp Thr Asp Thr Thr Val Tyr Ser Ser Glu Glu Ala Glu Leu Leu Lys
        1315                1320                1325
Leu Ile Glu Ile Gly Val Gln Thr Gly Ser Thr Ala Gln Ile Leu Gln
    1330                1335                1340
Pro Asp Xaa Gly Thr Thr Leu Ser Ser Pro Pro Val
1345                1350                1355
```

<210> 314
<211> 1298
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 24, 134
<223> Xaa = D or G

<220>
<221> VARIANT
<222> 149
<223> Xaa = N or D

<220>
<221> VARIANT
<222> 494
<223> Xaa = T or A

<220>
<221> VARIANT
<222> 854
<223> Xaa = G or S

<220>
<221> VARIANT
<222> 890
<223> Xaa = Q or H

<220>
<221> VARIANT
<222> 915
<223> Xaa = A or P

<220>
<221> VARIANT
<222> 916
<223> Xaa = C or W

<220>
<221> VARIANT
<222> 933
<223> Xaa = G or R

<220>
<221> VARIANT
<222> 954
<223> Xaa = P or S

<220>
<221> VARIANT
<222> 1008
<223> Xaa = P or L

<220>
<221> VARIANT
<222> 1041
<223> Xaa = R or Q

<220>
<221> VARIANT
<222> 1137
<223> Xaa = P or L

<220>
<221> VARIANT
<222> 1164
<223> Xaa = D or E

<220>
<221> VARIANT
<222> 1189
<223> Xaa = R or L

<220>
<221> VARIANT
<222> 1324
<223> Xaa = R or L

<400> 314
Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
1 5 10 15
Leu Leu Asp Gly Leu Val Ser Xaa Tyr Ser Met Thr Pro Pro Thr Leu
20 25 30
Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
35 40 45
Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
50 55 60
Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65 70 75 80
Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
85 90 95
Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110
Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
115 120 125
Tyr Val Phe Val Arg Xaa Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
130 135 140
Thr Leu Leu Val Xaa Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145 150 155 160
Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
165 170 175
Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
180 185 190
Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
195 200 205
Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
210 215 220
Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225 230 235 240
Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
245 250 255
Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
260 265 270
Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His

```
        275                 280                 285
Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
    290                 295                 300
Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305                 310                 315                 320
Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
                325                 330                 335
Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
            340                 345                 350
Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
        355                 360                 365
Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
    370                 375                 380
Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385                 390                 395                 400
Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
                405                 410                 415
Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
            420                 425                 430
Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
        435                 440                 445
Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr
    450                 455                 460
Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465                 470                 475                 480
Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Xaa Gln Asp
                485                 490                 495
Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
            500                 505                 510
Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
        515                 520                 525
Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
    530                 535                 540
Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile
545                 550                 555                 560
Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
                565                 570                 575
Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
            580                 585                 590
Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
        595                 600                 605
Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
    610                 615                 620
Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
625                 630                 635                 640
Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
                645                 650                 655
Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
            660                 665                 670
Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
        675                 680                 685
Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
    690                 695                 700
His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705                 710                 715                 720
Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
```

```
                725                 730                 735
Arg Val Arg Glu Glu Asp Ala Gly Pro Tyr Leu Cys Ser Val Cys Arg
            740                 745                 750
Pro Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser
        755                 760                 765
Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val
    770                 775                 780
Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met
785                 790                 795                 800
Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile
                805                 810                 815
Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser
            820                 825                 830
Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
        835                 840                 845
Arg Val Leu Gly Tyr Xaa Ala Phe Gly Lys Val Val Glu Ala Ser Ala
    850                 855                 860
Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met
865                 870                 875                 880
Leu Lys Glu Gly Ala Thr Ala Ser Glu Xaa Arg Ala Leu Met Ser Glu
                885                 890                 895
Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu
            900                 905                 910
Leu Gly Xaa Xaa Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu
        915                 920                 925
Phe Cys Lys Tyr Xaa Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp
    930                 935                 940
Ala Phe Ser Pro Cys Ala Glu Lys Ser Xaa Glu Gln Arg Gly Arg Phe
945                 950                 955                 960
Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser
                965                 970                 975
Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala
            980                 985                 990
Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Xaa
        995                 1000                1005
Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg Gly
    1010                1015                1020
Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala
1025                1030                1035                1040
Xaa Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile Cys Asp Phe
                1045                1050                1055
Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
            1060                1065                1070
Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asp
        1075                1080                1085
Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
    1090                1095                1100
Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile
1105                1110                1115                1120
Asn Glu Glu Phe Cys Gln Arg Val Arg Asp Gly Thr Arg Met Arg Ala
                1125                1130                1135
Xaa Glu Leu Ala Thr Pro Ala Ile Arg His Ile Met Leu Asn Cys Trp
            1140                1145                1150
Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Xaa Leu Val Glu Ile
        1155                1160                1165
Leu Gly Asp Leu Leu Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val
```

```
    1170                1175                1180
Cys Met Ala Pro Xaa Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser
1185                1190                1195                1200
Gln Val Ser Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp
                1205                1210                1215
Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn
            1220                1225                1230
Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
        1235                1240                1245
Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr Thr
    1250                1255                1260
Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala
1265                1270                1275                1280
Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln Glu Ser Gly
                1285                1290                1295
Phe Arg
```

<210> 315
<211> 27
<212> DNA
<213> synthetic

<400> 315
ccatgggcgg cggcggctct gccatgg 27

<210> 316
<211> 42
<212> DNA
<213> synthetic

<400> 316
ccatgggcgg cggcggctct ggcggcggcg gctctgccat gg 42

<210> 317
<211> 75
<212> DNA
<213> synthetic

<400> 317
ccatggcctc gtcgtcgtcg ggctcgtcgt cgtcgggctc gtcgtcgtcg ggctcgtcgt 60
cgtcgggcgc catgg 75

<210> 318
<211> 45
<212> DNA
<213> synthetic

<400> 318
ccatggcctc gtcgtcgtcg ggctcgtcgt cgtcgggcgc catgg 45

<210> 319
<211> 8
<212> PRT
<213> synthetic

<400> 319
Ala Ala Pro Ala Ala Ala Pro Ala
1 5

<210> 320
<211> 419
<212> PRT
<213> Homo sapiens

<400> 320
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
340 345 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser

```
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Asp Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Ser Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 321
<211> 79
<212> PRT
<213> Homo sapiens

```
<400> 321
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75
```

<210> 322
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 342
<223> Xaa= Thr or Ser

```
<400> 322
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
```

```
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Xaa His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 323
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 345
<223> Xaa= Leu or Pro

<400> 323

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
```

```
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Xaa Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 324
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 346
<223> Xaa= Pro or Leu

<400> 324
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu

```
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Xaa Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 325
<211> 419
<212> PRT

<213> Homo sapiens

<220>
<221> VARIANT
<222> 356
<223> Xaa= Leu or Gln

<400> 325

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Xaa Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
```

```
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly

<210> 326
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 358
<223> Xaa= Met or Leu

<400> 326
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
```

305 310 315 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
340 345 350
Pro Val Pro Leu Arg Xaa Gln Pro Gly Pro Ala His Pro Val Leu Ser
355 360 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
370 375 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385 390 395 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
405 410 415
Tyr Glu Gly

<210> 327
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 361
<223> Xaa= Gly, Asp, Ala, or Val

<400> 327
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240

```
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Xaa Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 328
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 376
<223> Xaa= Leu or Ile

<400> 328

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
```

```
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Xaa Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly

<210> 329
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 394
<223> Xaa= Pro or Arg

<400> 329
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
```

```
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Xaa Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly

<210> 330
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 404
<223> Xaa= Pro or Leu

<400> 330
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
```

```
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Xaa Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 331
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 413
<223> Xaa= Asp or Asn

<400> 331
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
340 345 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
355 360 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
370 375 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val

385 390 395 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Xaa Leu Ser Arg
405 410 415
Tyr Glu Gly

<210> 332
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 357
<223> Xaa= Arg or Cys

<400> 332
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305 310 315 320

```
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Xaa Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Arg Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 333
<211> 419
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 371
<223> Xaa= Arg or Ile

```
<400> 333
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
 1               5                  10                  15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
            20                  25                  30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
        35                  40                  45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
```

```
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val
            340                 345                 350
Pro Val Pro Leu Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser
        355                 360                 365
Phe Leu Xaa Pro Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro
    370                 375                 380
Leu Ala Pro Leu Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val
385                 390                 395                 400
Gly Arg Gly Pro Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg
                405                 410                 415
Tyr Glu Gly
```

<210> 334
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 2
<223> Xaa= Thr or Ser

<400> 334

```
Gly Xaa His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75
```

<210> 335
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 5
<223> Xaa= Leu or Pro

<400> 335

```
Gly Thr His Ser Xaa Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 336
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 6
<223> Xaa= Pro or Leu

<400> 336
Gly Thr His Ser Leu Xaa Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 337
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 16
<223> Xaa= Leu or Gln

<400> 337
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Xaa
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 338
```

<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 18
<223> Xaa= Met or Leu

<400> 338
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
1 5 10 15
Arg Xaa Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
20 25 30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
35 40 45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
50 55 60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65 70 75

<210> 339
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 21
<223> Xaa= Gly, Asp, Ala, or Val

<400> 339
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
1 5 10 15
Arg Met Gln Pro Xaa Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
20 25 30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
35 40 45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
50 55 60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65 70 75

<210> 340
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 36
<223> Xaa= Leu or Ile

<400> 340
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu

```
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Xaa Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 341
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 54
<223> Xaa= Pro or Arg

<400> 341
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Xaa Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 342
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 64
<223> Xaa= Pro or Leu

<400> 342
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
 1               5                  10                  15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Xaa
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75

<210> 343
<211> 79
```

<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 73
<223> Xaa= Asp or Asn

<400> 343
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
1 5 10 15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
20 25 30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
35 40 45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
50 55 60
Asp Pro Asp Ala His Val Ala Val Xaa Leu Ser Arg Tyr Glu Gly
65 70 75

<210> 344
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 17
<223> Xaa= Arg or Cys

<400> 344
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
1 5 10 15
Xaa Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Arg Pro
20 25 30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
35 40 45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
50 55 60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65 70 75

<210> 345
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> 31
<223> Xaa= Arg or Ile

<400> 345
Gly Thr His Ser Leu Pro Pro Arg Pro Ala Ala Val Pro Val Pro Leu
1 5 10 15
Arg Met Gln Pro Gly Pro Ala His Pro Val Leu Ser Phe Leu Xaa Pro

```
            20                  25                  30
Ser Trp Asp Leu Val Ser Ala Phe Tyr Ser Leu Pro Leu Ala Pro Leu
        35                  40                  45
Ser Pro Thr Ser Val Pro Ile Ser Pro Val Ser Val Gly Arg Gly Pro
    50                  55                  60
Asp Pro Asp Ala His Val Ala Val Asp Leu Ser Arg Tyr Glu Gly
65                  70                  75
```

<210> 346
<211> 240
<212> DNA
<213> Homo sapiens

<400> 346
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 347
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 4
<223> n= T

<400> 347
ggtncccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 348
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 14
<223> n= C

<400> 348
ggtacccact cacngccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 349
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 17
<223> n= T

<400> 349
ggtacccact cactgcnccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 350
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 47
<223> n= A

<400> 350
ggtacccact cactgccccc gaggccagct gcagttcctg tccctcngcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 351
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 54
<223> n= A

<400> 351
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catncagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 352
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 62
<223> n= C, T, or A

<400> 352

ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
gncccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 353
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 106
<223> n= A

<400> 353
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacntagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 354
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 161
<223> n= C

<400> 354
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ntatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 355
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 191
<223> n= T

<400> 355
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc nggaccctga tgctcatgtg gctgttgacc tgtcccggta tgaaggctga 240

<210> 356

<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 217
<223> n= C

<400> 356
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttnacc tgtcccggta tgaaggctga 240

<210> 357
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 17
<223> n= T

<220>
<221> misc_feature
<222> 217
<223> n= C

<400> 357
ggtacccact cactgcnccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttnacc tgtcccggta tgaaggctga 240

<210> 358
<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 49
<223> n= T

<400> 358
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgng catgcagcct 60
ggcccagccc accctgtcct atccttcctc agaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttnacc tgtcccggta tgaaggctga 240

<210> 359

<211> 240
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 92
<223> n= T

<400> 359
ggtacccact cactgccccc gaggccagct gcagttcctg tccctctgcg catgcagcct 60
ggcccagccc accctgtcct atccttcctc anaccctctt gggacctagt ctctgccttc 120
tactctctac ccctggcccc cctcagccct acaagtgtcc ctatatcccc tgtcagtgtg 180
gggaggggcc cggaccctga tgctcatgtg gctgttnacc tgtcccggta tgaaggctga 240