COMPOSITIONS MONOVALENT FOR CD28 BINDING AND METHODS OF USE

REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 61/162,121, filed March 20, 2009, and U.S. Provisional Application No. 61/082,078, filed July 18, 2008.

FIELD OF THE INVENTION

Domain antibodies (dAbs) that bind CD28 and prevent the binding of CD28 to CD80 and/or CD86, wherein the dAbs do not cross-react with CTLA4, and methods of using the same are provided.

SEQUENCE LISTING

The Sequence Listing attached below is incorporated herein by reference.

BACKGROUND

Antigen-nonspecific intercellular interactions between T-lymphocytes and antigen-presenting cells (APCs) generate T cell co-stimulatory signals that generate T cell responses to antigen (Jenkins and Johnson (1993) *Curr. Opin. Immunol.* 5: 361-367). Co-stimulatory signals determine the magnitude of a T cell response to antigen and whether this response activates or inactivates subsequent responses to antigen (Mueller et al. (1989) *Annu. Rev. Immunol.* 7: 445- 480). T cell activation in the absence of co-stimulation results in an aborted or anergic T cell response (Schwartz, R. H. (1992) *Cell* 71: 1065-1068). One key co-stimulatory signal is provided by interaction of the T cell surface receptor CD28 with B7-related molecules on antigen presenting cells (e.g., B7-1 and B7-2, or CD80 and CD86, respectively) (P. Linsley and J. Ledbetter (1993) *Annu. Rev. Immunol.* 11: 191-212). The interaction of CD28 with B7-1 (CD80) and B7-2 (CD86) co-stimulatory molecules provides a major signaling pathway for augmenting and sustaining T cell responses (Freedman et al. (1987) *J. Immunol.* 137: 3260-3267; Freeman et al. (1989) J. *Immunol.* 143: 2714-2722; Freeman et al. (1991) *J. Exp. Med.* 174: 625-631; Freeman et al. (1993) *Science* 262: 909-911; Azuma et al. (1993) *Nature* 366: 76-79; Freeman et al. (1993) *J. Exp. Med.* 178: 2185-2192).

CD28 is constitutively expressed on the surface of T cells, virtually all human CD4+ T cells, to a lesser extent on human CD8 + T cells, some natural killer cells and all murine T cells. CD28 is a type I transmembrane glycoprotein and is a member of the Immunoglobulin family by virtue of its single Ig variable-like extracellular domain which has a MYPPPY (SEQ ID NO: 639) motif required for binding CD80 and CD86 (Peach et al. 1994, *J. Exp. Med.* 180: 2049-2058). CD28 has a cysteine residue located after the Ig variable-like domain, which is involved in its homodimerization. The protein sequence of CD28 and a nucleic acid encoding a human CD28 are disclosed, for example, in Harper et al. *J. Immunol.* (1991) 147: 1037-44. The sequence of a human mRNA encoding CD28 also is disclosed in NCBI Accession No. NM_006139, last updated April 19, 2009, for example. The complete protein sequence of a human CD28 also is disclosed in NCBI Accession No. NP_006130, last updated April 19, 2009, for example.

CD28 transmits a signal that synergizes with the T cell receptor (TCR) signal to promote the activation of naïve T cells (Lanzavecchia et al. (1999) *Cell* 96: 1-4). CD28 signaling regulates the threshold for T cell activation and significantly reduces the number of TCR engagements needed for effective T cell activation (Viola et al. (1996) *Science* 273: 104-6). CD28 co-stimulation results in enhanced T cell proliferation, production of multiple cytokines and cytokine receptors, increased expression of proteins involved in cell cycle progression, sustaining T cell survival, and sustained CD40Ligand (CD40L) expression on T cells (Sharpe et al. *Fundamental Immunology*, W.E. Paul Ed. Fifth Edition, Page 396).

CD28 signals have a critical role in regulating CD4 and CD8 T cell differentiation. CD28 also optimizes the responses of previously activated T cells, promoting IL-2 production and T cell survival. IL-4 production by naïve T cells is highly dependent on B7-1/B7-2 co-stimulation. Interruption of the CD28/B7 pathway during activation of naïve T cells impairs T cell proliferation and differentiation, while interruption of the CD28/B7 pathway in previously activated T cells diminishes T cell expansion but not effector cytokine production (Sharpe et al. *Fundamental Immunology*, W.E. Paul Ed. Fifth Edition, pages 393-404).

T helper cell-dependent antibody responses use the B7-CD28 pathway to provide co-stimulatory signals essential for cognate T cell/B cell interactions required for Immunoglobulin class switching and germinal center formation. In CD28 knock-out mice, potentially reactive B cells accumulate within lymphoid follicles after antigenic

stimulation, but are not able to proliferate or undergo somatic mutation, (Ferguson et al. (1996) *J. Immunol.* 156: 4576-4581).

B7-1 and B7-2 are also ligands for a second, higher affinity receptor, CTLA4 (CD152), which is present on the surface of activated T cells. B7-1/B7-2 co-stimulation of inhibitory signals occurs when B7-1/B7-2 bind CTLA-4 (Brunet et al. (1987) *Nature* 328: 267-270, Linsley et al. (1991) *J. Exp. Med.*174: 561-569). The outcome of an immune response involves a balance between CD28 mediated T cell activation and CTLA-4 mediated T cell inhibition.

Inhibition of CD28 mediated T cell activation could inhibit undesired T cell responses occurring during autoimmunity, transplant rejection, or allergic responses. For example, inhibiting CD28 mediated T cell activation could delay graft rejection, prevent acute allograft rejection, induce donor specific tolerance, and prevent development and interrupt the progression of chronic allograft rejection, as well as prevent graft versus host disease (GVH), i.e., when transplanted T cells mount a vigorous immune response against host tissue alloantigens (Salama et al. (2001) *J. Clin. Invest.* 108: 943-48). Not only would inhibiting CD28 mediated T cell activation dampen the immune response through negating activation signaling through CD28, it should not impact the interaction of CD86 and CD80 to CTLA-4, thereby preserving CTLA-4 mediated inhibition of the T cell response. Thus, inhibiting CD28 mediated T cell activation could be used to prevent induction of autoimmunity and moderate the progression and/or severity of established autoimmune diseases, including models of collagen induced arthritis, autoimmune thyroiditis, autoimmune uveitis, myasthenia gravis and lupus (Saloman et al. (2001) *Ann. Rev. Immunol.* 19: 225-252).

What is needed is a way to inhibit CD28-mediated T cell activation, without stimulation of CD28 signaling pathways. The disclosure set forth herein meets and addresses this need.

SUMMARY

Provided herein are domain antibodies (dAbs) that monovalently bind CD28. Because of the clear importance of CD28 in the regulation of the T cell response and the production of antibodies, the CD28/B7 (CD80 and CD86) interaction and pathways present important targets for the development of therapeutic approaches for the treatment of diseases and disorders that involve inappropriate cellular responses, such as transplant

rejection, autoimmunity, and/or excessive antibody responses. Domain antibodies that are monovalent for binding of CD28 can inhibit CD28 activity, dampening an immune response, while avoiding potential undesirable effects that can occur with antibodies capable of divalent or multivalent binding of CD28. Domain antibodies can also be applied to any of a number of uses for which standard divalent antibodies are also used, e.g., *in vivo* imaging and diagnosis.

Accordingly, described herein are domain antibodies that bind CD28 and prevent or inhibit the binding of CD28 to CD80, CD86 and/or other ligands and inhibit CD28 signaling by CD80 and/or CD86 in receptor binding assays. Domain antibodies described herein also do not block the interaction of CD80 and CD86 to CTLA4. In an embodiment, domain antibodies described herein do not cross-react with CTLA4, and thus do not bind the common motif on CTLA4 and CD28 that binds CD80/86.

In one embodiment, the binding of the domain antibody to CD28 does not substantially agonize CD28 activity. In particular, the dAb does not agonize CD28 signaling in combination with T cell receptor signaling. In another embodiment, the domain antibody inhibits the binding of CD28 to CD80. In another embodiment, the domain antibody inhibits the binding of CD28 to CD80, and does not substantially agonize signaling by CD28. In yet another embodiment, the domain antibody inhibits the binding of CD28 to CD86. In another embodiment, the domain antibody inhibits the binding of CD28 to CD86, and does not substantially agonize signaling by CD28. Also included is a dAb that interferes with the binding of CD80 and/or CD86 to the MYPPPY (SEQ ID NO: 639) sequence of CD28

In an aspect, the dAb does not substantially induce T cell proliferation in combination with T cell receptor signaling. In another aspect, the dAb does not substantially induce cytokine secretion by T cells in combination with T cell receptor signaling. In an embodiment, a cytokine is at least one cytokine selected from the group consisting of GM-CSF, IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-12 IL-13, IL-15, IL-17, IL-21, IL-22, IL-24, TGFβ, TNF-α, TNF-β, IFN-α, IFN-β, IFN-γ.

In one aspect, because human antibodies will avoid the generation of an immune response to the antibodies when administered to human subjects for the treatment or prevention of disease, the domain antibody is a human domain antibody that

monovalently binds CD28, and in an exemplary embodiment, without substantially agonizing CD28 activity.

In one embodiment, the domain antibody interacts with human CD28 with a K_d in the range of 50 nM to 1 pM, inclusive, as measured by surface plasmon resonance. For example, the K_d for human CD28 can be 25 nM to 20 pM, 10 nM to 20 pM, 5 nm to 20 pM, 1 nM to 20 pM, 0.5 nM to 20 pM, 0.1 nM to 20 pM, 0.1 nM to 50 pM, 75 pM to 20 pM, or even 50 pM to 20 pM. In an embodiment, the K_d for human CD28 is about 50 pM.

In one embodiment, the domain antibody inhibits binding of CD80 to CD28 with an IC_{50} of 50nM or less. In one embodiment, the domain antibody inhibits binding of CD86 to CD28 with an IC_{50} of 50nM or less. In a further embodiment, the domain antibody has binding specificity to CD28 with a K_{off} rate constant of $1x10^{-3}$ s^{-1} or less, $1x10^{-4}$ s^{-1} or less, $1x10^{-5}$ s^{-1} or less, or $1x10^{-6}$ s^{-1} or less, as determined by surface plasmon resonance. In one embodiment, the domain antibody neutralizes CD28 in a standard assay with a IC_{50} of 50nM or less.

In another embodiment, the domain antibody comprises a single immunoglobulin variable domain that binds CD28. In one embodiment, the single immunoglobulin variable domain is a V_H or a V_L domain. In another embodiment, the domain antibody comprises a homomultimer or heteromultimer of two variable domains, e.g., a V_H and V_L domain, but one of the variable domains has the capacity to bind CD28 without the need for a corresponding V_L or V_H domain. That is, the dAb binds antigen independently of the additional V_H or V_L domains. The variable domains in these embodiments may comprise three complementarity determining regions (CDRs). In another embodiment, the domain antibody is free of an Fc domain. The limits of an Fc domain are set out in Kabat et al. (1991, Sequences of Immunological Interest, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.; incorporated herein by reference). In the alternative, an Fc domain consists of the CH2-CH3 regions, optionally including a hinge region linked to the CH2.

In one aspect, the domain antibody comprises a universal framework. In this aspect, a domain antibody may comprise one or more framework regions comprising an amino acid sequence that is the same as the amino acid sequence of a corresponding framework (FW) region encoded by a human germline antibody gene segment, or the

amino acid sequence of one or more of said framework regions collectively comprising up to 5, *e.g.*, 1, 2, 3, 4 or 5, amino acid differences relative to the amino acid sequence of said corresponding framework region encoded by a human germline antibody gene segment.

In one embodiment, the dAb comprises amino acid sequences of FW1, FW2, FW3, and FW4 that correspond to the FW1, FW2, FW3, and FW4 of a human antibody, e.g., a human germline antibody. In a further embodiment, some or all of the amino acid sequences of FW1, FW2, FW3, and FW4 of the domain antibody are the same as the amino acid sequences of corresponding framework regions encoded by human germline antibody gene segments. For example, FW2 may be identical to the FW2 of a human antibody. In another embodiment, the amino acid sequences of FW1, FW2, FW3, and FW4 collectively contain up to 10 amino acid differences relative to the amino acid sequences of corresponding framework regions encoded by said human germline antibody gene segment. In a further embodiment of the foregoing, the human germline antibody gene segment can be selected from the group consisting of DP47, DP45, DP48, and DPK9. In one embodiment, the universal framework comprises a V_H framework selected from the group consisting of DP47, DP45, and DP38, and/or the V_L framework is DPK9.

In one aspect, a domain antibody is formatted to increase its *in vivo* half-life. In particular, the domain antibody has an increased *in vivo* t-α or t-β half-life relative to the same unformatted domain antibody.

In one embodiment, the tα-half-life of the domain antibody composition is increased by 10% or more when compared to an unmodified protein assayed under otherwise identical conditions. In another embodiment, the tα-half-life of the domain antibody composition is increased by 50% or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 2X or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 5X or more, e.g., 10X, 15X, 20X, 25X, 30X, 40X, 50X, or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 100X, 200X, 300X, 400X, 500X, or more.

In another embodiment, the domain antibody has a tα half-life of 0.25 to 6 hours, inclusive. In another embodiment, the tα half-life is in the range of 30 minutes to 12

hours, inclusive. In another embodiment, the tα-half-life of the domain antibody is in the range of 1 to 6 hours.

In another embodiment, the tβ-half-life of the domain antibody is increased by 10% or more when compared to an unmodified protein assayed under otherwise identical conditions. In another embodiment, the tβ-half-life of the domain antibody is increased by 50% or more. In another embodiment, the tβ-half-life of the antibody domain antibody is increased by 2X or more. In another embodiment, the tβ-half-life of the domain antibody is increased by 5X or more, e.g., 10X, 15X, 20X, 25X, 30X, 40X, or more. In another embodiment, the tβ-half-life of the domain antibody is increased by 50X or more.

In another embodiment, the domain antibody has a tβ half-life of 1 hour to 744 hours, inclusive. In another embodiment, the tβ-half-life is in the range of 12 to 48 hours, inclusive. In another embodiment, the tβ half-life is in the range of 12 to 26 hours, inclusive. In yet another embodiment, the tβ half-life is about 336 hours.

In addition to, or alternative to the above criteria, a domain antibody-containing composition is provided comprising a ligand having an AUC value (area under the curve) in the range of 1 mg·min/ml or more. In one embodiment, the lower end of the range is 5, 10, 15, 20, 30, 100, 200, or 300 mg·min/ml. In addition, or alternatively, a ligand or composition has an AUC in the range of up to 600 mg·min/ml. In one embodiment, the upper end of the range is 500, 400, 300, 200, 150, 100, 75, or 50 mg·min/ml. Advantageously a ligand will have an AUC in the range selected from the group consisting of the following: 15 to 150 mg·min/ml, 15 to 100 mg·min/ml, 15 to 75 mg·min/ml, and 15 to 50 mg·min/ml.

In one formatting embodiment, the domain antibodies described herein can be linked to human serum albumin (HSA), which also has the effect of increasing the *in vivo* half-life of the molecule. The human serum albumin coding sequences can be obtained by PCR using primers derived from the cDNA sequence available at GenBank Accession No. NM000477. Such coding sequences can be fused to the coding sequence for a domain antibody as described herein, and the fusion can be expressed by one of skill in the art.In one embodiment, the tα-half-life of the HSA-linked domain antibody composition is increased by 10% or more. In another embodiment, the tα-half-life of the HSA-linked domain antibody composition is in the range of 0.25 hours to 6 hours. In

another embodiment, the tβ-half-life of the HSA-linked domain antibody composition is increased by 10% or more. In another embodiment, the tβ-half-life of the HSA-linked domain antibody composition is in the range of 12 to 48 hours.

In another embodiment, the formatting comprises PEGylation of the dAb. In one embodiment, the PEG is covalently linked. In another embodiment, the PEG is linked to the domain antibody at a cysteine or lysine residue. In yet another embodiment, the PEG-linked domain antibody has a hydrodynamic size of at least 24 kD. In yet another embodiment, the total PEG size is from 20 to 60 kD, inclusive. In yet another embodiment, the PEG-linked domain antibody has a hydrodynamic size of at least 200 kD.

In another embodiment, the PEG-linked domain antibody has an increased *in vivo* half-life relative to the same polypeptide composition lacking linked polyethylene glycol. In another embodiment, the tα-half-life of the domain antibody composition is increased by 10% or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 50% or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 2X or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 5X or more, e.g., 10X, 15X, 20X, 25X, 30X, 40X, 50X, or more. In another embodiment, the tα-half-life of the domain antibody composition is increased by 100X, 200X, 300X, 400X, 500X, or more.

In another embodiment, the PEG-linked domain antibody has a tα half-life of 0.25 to 6 hours, inclusive. In another embodiment, the tα half-life is in the range of 30 minutes to 12 hours, inclusive. In another embodiment, the tα-half-life of the domain antibody is in the range of 1 to 6 hours.

In another embodiment, the tβ-half-life of the PEG-linked domain antibody is increased by 10% or more. In another embodiment, the tβ-half-life of the PEG-linked domain antibody is increased by 50% or more. In another embodiment, the tβ-half-life of the PEG-linked domain antibody is increased by 2X or more. In another embodiment, the tβ-half-life of the PEG-linked domain antibody is increased by 5X or more, e.g., 10X, 15X, 20X, 25X, 30X, 40X, or more. In another embodiment, the tβ-half-life of the PEG-linked domain antibody is increased by 50X or more.

In another embodiment, the PEG-linked domain antibody has a tβ half-life of 1 to 170 hours, inclusive. In another embodiment, the tβ-half-life is in the range of 12 to 48 hours, inclusive. In another embodiment, the tβ-half-life is in the range of 12 to 26 hours, inclusive.

In another embodiment, the PEG-linked domain antibody has an AUC value (area under the curve) in the range of 1 mg.min/ml or more. In one embodiment, the lower end of the range is about 5, 10, 15, 20, 30, 100, 200, or 300 mg·min/ml. In addition, or alternatively, a ligand or composition has an AUC in the range of up to about 600 mg·min/ml. In one embodiment, the upper end of the range is about 500, 400, 300, 200, 150, 100, 75, or 50 mg·min/ml. Advantageously a ligand will have an AUC in the range selected from the group consisting of the following: about 15 to 150 mg·min/ml, about 15 to 100 mg·min/ml, about 15 to 75 mg·min/ml, and about 15 to 50 mg·min/ml.

In another embodiment is provided a domain antibody which has an amino acid sequence at least 85% identical, e.g., at least 90% identical, at least 95% identical, and up to and including 96%, 97%, 98%, or 99% identical, to an amino acid sequence encoded by a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOS:1-57, which domain antibody specifically and monovalently binds CD28.

In another embodiment, the domain antibody comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:58-398 and 640,and SEQ ID NOs:532-635, and in an exemplary embodiment, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622.

In yet another aspect, domain antibody is provided for which has an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:58, SEQ ID

NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622, which polypeptide specifically and monovalently binds CD28. In another embodiment, a domain antibody differs from the selected amino acid sequence at no more than 25 amino acid positions and has a sequence that is at least 80% identical to the selected sequence. In one embodiment, the domain antibody differs from the selected amino acid sequence at 25 or fewer amino acid positions, 20 or fewer amino acid positions, 15 or fewer amino acid positions, 10 or fewer amino acid positions, 5 or fewer amino acid positions, 2 or fewer amino acid positions, or as few as one amino acid position. In a further embodiment, the domain antibody is at least 80% identical to the selected sequence, for example, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, at least 95% identical, and up to and including 96%, 97%, 98%, or 99% identical.

In one embodiment, a CD28 antagonist has a CDR1 sequence that is at least 50% identical to the CDR1 sequence of the amino acid sequence selected from the group consisting of SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622.

In one embodiment, the CDR1 differs from the selected amino acid sequence at all CDR1 amino acid positions, 5 or fewer amino acid positions, 4 or fewer amino acid positions, 3 or fewer amino acid positions, 2 or fewer amino acid positions, or as few as

one amino acid position. In a further embodiment, the CDR1 is at least 50% identical to the selected sequence, for example, at least 60% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, at least 95% identical, and up to and including 96%, 97%, 98%, or 99% identical.

In one embodiment, a CD28 antagonist has a CDR2 sequence that is at least 50% identical to the CDR2 sequence of the amino acid sequence selected from the group consisting of SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622.

In one embodiment, the CDR2 differs from the selected amino acid sequence at all CDR2 amino acid positions, 5 or fewer amino acid positions, 4 or fewer amino acid positions, 3 or fewer amino acid positions, 2 or fewer amino acid positions, or as few as one amino acid position. In a further embodiment, the CDR2 is at least 50% identical to the selected sequence, for example, at least 60% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, at least 95% identical, and up to and including 96%, 97%, 98%, or 99% identical.

In one embodiment, a CD28 antagonist has a CDR3 sequence that is at least 50% identical to the CDR2 sequence of the amino acid sequence selected from the group consisting of SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622.

In one embodiment, the CDR3 differs from the selected amino acid sequence at all CDR3 amino acid positions, 5 or fewer amino acid positions, 4 or fewer amino acid positions, 3 or fewer amino acid positions, 2 or fewer amino acid positions, or as few as one amino acid position. In a further embodiment, the CDR2 is at least 50% identical to the selected sequence, for example, at least 60% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, at least 95% identical, and up to and including 96%, 97%, 98%, or 99% identical.

Further included is a dAb comprising a CDR1 sequence at least 50 % identical to one of the CDR1 sequences selected from the group consisting of SEQ ID NO:484, SEQ ID NO:487, SEQ ID NO:490, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:499, SEQ ID NO:502, SEQ ID NO:505, SEQ ID NO:508, SEQ ID NO:511, SEQ ID NO:514, SEQ ID NO:517, SEQ ID NO:520, SEQ ID NO:523, SEQ ID NO:526, SEQ ID NO:529 and SEQ ID NO:636; a CDR2 sequence at least 50 % identical to one of the CDR2 sequences selected from the group consisting of SEQ ID NO:485, SEQ ID NO:488, SEQ ID NO:491, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:500, SEQ ID NO:503, SEQ ID NO:506, SEQ ID NO:509, SEQ ID NO:512, SEQ ID NO:515, SEQ ID NO:518, SEQ ID NO:521, SEQ ID NO:524, SEQ ID NO:527, SEQ ID NO:530 and SEQ ID NO:637; and a CDR3 sequence at least 50% identical to one of the CDR3 sequences selected from the group consisting of SEQ ID NO:486, SEQ ID NO:489, SEQ ID NO:492, SEQ ID NO:495, SEQ ID NO:498, SEQ ID NO:501, SEQ ID NO:504, SEQ ID NO:507, SEQ ID NO:510, SEQ ID NO:513, SEQ ID NO:516, SEQ ID NO:519, SEQ ID NO:522, SEQ ID NO:525, SEQ ID NO:528, SEQ ID NO:531 and SEQ ID NO:638.

In another aspect, included is a dAb comprising a CDR1 sequence selected from the group consisting of SEQ ID NO:484, SEQ ID NO:487, SEQ ID NO:490, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:499, SEQ ID NO:502, SEQ ID NO:505, SEQ ID NO:508, SEQ ID NO:511, SEQ ID NO:514, SEQ ID NO:517, SEQ ID NO:520, SEQ ID NO:523, SEQ ID NO:526, SEQ ID NO:529 and SEQ ID NO:636; a CDR2 sequence selected from the group consisting of SEQ ID NO:485, SEQ ID NO:488, SEQ ID NO:491, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:500, SEQ ID NO:503, SEQ ID NO:506, SEQ ID NO:509, SEQ ID NO:512, SEQ ID NO:515, SEQ ID NO:518, SEQ ID NO:521, SEQ ID NO:524, SEQ ID NO:527, SEQ ID NO:530 and SEQ ID NO:637; and a CDR3 sequence selected from the group consisting of SEQ ID NO:486, SEQ ID NO:489, SEQ ID NO:492, SEQ ID NO:495, SEQ ID NO:498, SEQ ID NO:501, SEQ ID NO:504,

SEQ ID NO:507, SEQ ID NO:510, SEQ ID NO:513, SEQ ID NO:516, SEQ ID NO:519, SEQ ID NO:522, SEQ ID NO:525, SEQ ID NO:528, SEQ ID NO:531and SEQ ID NO:638.

In yet another aspect, a dAb comprises the amino acid sequence selected from the group consisting of SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:472, SEQ ID NO:473, SEQ ID NO:474, SEQ ID NO:475, SEQ ID NO:476, SEQ ID NO:477, SEQ ID NO:478, SEQ ID NO:479, SEQ ID NO:480, SEQ ID NO:481, SEQ ID NO:482, SEQ ID NO:483, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, and SEQ ID NO:622. In an embodiment, a dAb comprises an amino acid sequence that differs from that of SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:534, SEQ ID NO:535, SEQ ID NO:536, SEQ ID NO:537, SEQ ID NO:539, SEQ ID NO:540, SEQ ID NO:542, SEQ ID NO:543, SEQ ID NO:545, SEQ ID NO:547, SEQ ID NO:548, SEQ ID NO:550, SEQ ID NO:551, SEQ ID NO:553, SEQ ID NO:562, SEQ ID NO:567, SEQ ID NO:570, SEQ ID NO:575, SEQ ID NO:576, SEQ ID NO:577, SEQ ID NO:578, SEQ ID NO:580, SEQ ID NO:599, SEQ ID NO:600, SEQ ID NO:607, SEQ ID NO:611, SEQ ID NO:617, or SEQ ID NO:622 by no more than 25 amino acids.

The dAb may inhibit binding of CD28 to CD80 and/or CD86 with an IC_{50} of about 100 nM, about 50 nM, about 1 nM, about 500 pM, about 100 pM, about 50 pM, about 10 pM, about 5 pM, or about 1 pM. For example, the domain antibody inhibits binding of CD28 to CD80 with an IC_{50} in the range of 1 pM to 1.5 μM, inclusive; IC_{50} for inhibition of CD28 binding to CD80. The IC_{50} can be in the range of 1 pM to 1 μM, 1 pM to 900 nM, 1 pM to 800 nM, 1 pM to 700 nM, 1 pM to 600 nM, 1 pM to 500 nM, 1 pM to 400 nM, 1 pM to 300 nM, 1 pM to 200 nM, 1 pM to 100 nM, 1 pM to 50 nM, 1

pM to 10 nM, 1 pM to 1 nM, 1 pM to 500 pM, 1 pM to 100 pM, 1 pM to 50 pM, 1 pM to 10 pM, or 1 pM to 5 pM. Further acceptable ranges include, for example, 50 pM to 1 μM, 100 pM to 500 nM, 125 pM to 250 nM, 150 pM to 200 nM, 150 pM to 100 nM, and 200 pM to 50 nM.

In another embodiment, the domain antibody inhibits binding of CD28 to CD86 with an IC_{50} in the range of 1 pM to 1.5 μM, inclusive; IC_{50} for inhibition of CD28 binding to CD86. The IC_{50} can be in the range of 1 pM to 1 μM, 1 pM to 900 nM, 1 pM to 800 nM, 1 pM to 700 nM, 1 pM to 600 nM, 1 pM to 500 nM, 1 pM to 400 nM, 1 pM to 300 nM, 1 pM to 200 nM, 1 pM to 100 nM, 1 pM to 50 nM, 1 pM to 10 nM, 1 pM to 1 nM, 1 pM to 500 pM, 1 pM to 100 pM, 1 pM to 50 pM, 1 pM to 10 pM, or 1 pM to 5 pM. Further acceptable ranges include, for example, 50 pM to 1 μM, 100 pM to 500 nM, 125 pM to 250 nM, 150 pM to 200 nM, 150 pM to 100 nM, and 200 pM to 50 nM.

A method of antagonizing the binding of CD80 to CD28 in an individual is provided for, the method comprising administering a domain antibody as described herein to the individual, wherein the domain antibody antagonizes the binding of CD80 to CD28 in the individual. A method of antagonizing the binding of CD86 to CD28 in an individual comprises administering a domain antibody as described herein to the individual, wherein the domain antibody antagonizes the binding of CD86 to CD28 in the individual. A method of antagonizing an activity of CD28 in an individual comprises administering a domain antibody as described herein to the individual, wherein the domain antibody antagonizes an activity of CD28. A method of treating or preventing a disease or disorder mediated by CD28 in an individual in need of such treatment comprises administering to the individual a therapeutically effective amount of a composition comprising a domain antibody that binds CD28. In one embodiment, the disease or disorder is an autoimmune disease or disorder. In another embodiment, the disease or disorder is graft-related.

Also included is a dual specific ligand comprising a domain antibody having a binding specificity to a first antigen and a single variable domain having a binding activity to a second antigen, wherein the first antigen is CD28, and wherein binding of the single variable domain to the second antigen acts to increase the half-life of the ligand *in vivo*.

In one embodiment, the dual specific ligand is a four chain IgG immunoglobulin. The four chain IgG may comprise two dual specific ligands, said dual specific ligands being different in their variable domains.

In another embodiment, the domain antibodies are camelid V_{HH} domains. In this embodiment of the dual specific ligand, the single immunoglobulin variable domain may be a heavy chain variable domain. In another embodiment of the dual specific ligand, the single immunoglobulin variable domain is a light chain variable domain. In one embodiment of the dual specific ligand, the ligand is provided as an IgG immunoglobulin comprising four heavy chain single variable domains or four light chain single variable domains. The heavy chain can comprise camelid V_{HH} domains. In a further embodiment of the dual specific ligand, the first and second domains bind independently, such that the dual specific ligand may simultaneously bind both the first and second antigens. In one embodiment of the dual specific ligand, the domain antibody has a dissociation constant (K_d) of $1x10^{-8}$ M or less for human CD28, and a K_{off} rate constant of $1x10^{-3}$ s^{-1} or less, as determined by surface plasmon resonance.

In one embodiment of the dual specific ligand, the single variable domain is specific for serum albumin (SA) and has a dissociation constant (K_d) of 1nM to 500μm for SA, as determined by surface plasmon resonance. In a further embodiment, the single variable domain binds SA in a standard ligand binding assay with an IC50 of 1 nM to 500 μM. The single variable domain may be specific for SA, and comprise the amino acid sequence of MSA-16 or a sequence that is at least 80% identical thereto. Alternatively, the single variable domain may be specific for SA, and comprise the amino acid sequence of MSA-26 or a sequence that is at last 80% identical thereto.

In a further embodiment, the domain antibody can comprise a binding site for a generic ligand. In one embodiment, the generic ligand binding site is selected from the group consisting of protein A, protein L and protein G binding site.

In one embodiment of the dual specific ligand, the domain antibody comprises a universal framework. The domain antibody may also comprise a V_H framework selected from the group consisting of DP47, DP45 and DP38; or a V_L framework which is DPK9. The domain antibody may comprise one or more framework regions comprising an amino acid sequence that is the same as the amino acid sequence of a corresponding framework region encoded by a human germline antibody gene segment, or the amino

acid sequence of one or more of said framework regions collectively comprises up to 5 amino acid differences relative to the amino acid sequence of said corresponding framework region encoded by a human germline antibody gene segment.

In one embodiment, the amino acid sequences of FW1, FW2, FW3, and FW4 of the domain antibody are the same as the amino acid sequences of corresponding framework regions encoded by a human germline antibody gene segment, or the amino acid sequences of FW1, FW2, FW3, and FW4 collectively contain up to 10 amino acid differences relative to the amino acid sequences of corresponding framework regions encoded by said human germline antibody gene segment.

In one embodiment, the amino acid sequences of said FW1, FW2, and FW3 of the domain antibody are the same as the amino acid sequences of corresponding framework regions encoded by human germline antibody gene segments. The human germline antibody gene segments may be selected from the group consisting of DP47, DP45, DP48, and DPK9.

Also included is a method for producing a dual specific ligand as described herein, comprising a domain antibody having a binding specificity for CD28 and a single domain antibody having a binding specificity for a protein which increases the half-life of the ligand *in vivo*, the method comprising the steps of: selecting a first variable domain by its ability to bind CD28; selecting a second variable domain by its ability to bind to said protein which increases the half-life of the ligand *in vivo*; combining the variable domains; and selecting the dual specific ligand by its ability to bind to CD28 and said protein. In one embodiment, the domain antibody is selected for binding to CD28 in absence of a complementary variable domain.

Also included is nucleic acid encoding a dual specific ligand described herein. The nucleic acid may comprise the nucleic acid sequence of MSA-16 or a sequence that is at least 80% identical thereto, or alternatively may comprise, the nucleic acid sequence of MSA-26 or a sequence that is at least 70% identical thereto. The nucleic acid may be incorporated into a vector, which may be incorporated into a host cell.

Also included is a pharmaceutical composition comprising a dual specific ligand as described herein and a pharmaceutically acceptable excipient, carrier, or diluent.

Also included is a dual specific ligand comprising first and second heavy chain single variable domains, or first and second light chain single variable domains, wherein

the first variable domain is a domain antibody. In one embodiment, the second variable domain has binding specificity for an antigen other than CD28. In an aspect, the second variable domain contributes to and/or enhances the stability of a domain antibody. By way of a non-limiting example, the second variable domain has binding specificity serum albumin.

Also included is a dual specific ligand comprising a first single variable domain having a binding specificity to a first antigen and a second single variable domain having a binding activity to a second antigen, wherein the first antigen is CD28 and the second antigen is an antigen presenting cell surface antigen or a T cell surface antigen. The antigen presenting cell surface antigen can be selected from one of the group consisting of dendritic cell surface antigens, activated macrophage surface antigens, activated B cell surface antigens, co-stimulatory signal pathway surface antigens, and MHC antigens. In one embodiment, the MHC antigen is a MHC class II antigen, and the class II antigen can be the alpha and/or beta chain.

The antigen presenting cell surface antigen or a T cell surface antigen may be selected from the group consisting of CD40, CD40L, Inducible co-stimulatory molecule (ICOS), CD27, CD30, OX40, CD45, CD69, CD3, CD70, inducible co-stimulatory molecule ligand (ICOSL), OX40L, CD80, CD86, HVEM (Herpes Virus Entry Mediator), and LIGHT, including one of CD40L, Inducible co-stimulatory molecule (ICOS), CD27, CD30, OX40, CD45, CD69, or CD3. An exemplary surface antigen is a B7 gene surface antigen such as CD86 or CD80.

In another embodiment, a dual specific ligand comprises a first domain antibody having a binding specificity for a first antigen and a second single variable domain having a binding activity to a second antigen, wherein the first antigen is CD28 and the second antigen is a cytokine. In particular embodiments, the cytokine may be GM-CSF, IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-10, IL-11 IL-12 IL-13, IL-15, IL-17, IL-18, IL-21, IL-22, IL-23, IL-24, IL-28, IL-33, LIF, TGFβ, TNF-α, TNF-β, IFN-α, IFN-β, IFN-γ.

Domain antibodies as described herein also may be administered in combination with additional immunosuppressive/immunomodulatory and/or anti-inflammatory agents or therapies, such as a calcineuirin inhibitor, cyclosporine, cytoxan, prednisone, azathioprine, methotrexate, corticosteroids, nonsteroidal antiinflammatory drugs/Cox-2 inhibitors, hydroxychloroquine, sulphasalazopryine, gold salts, etanercept, infliximab,

anakinra, mizoribine, mycophenolic acid, mycophenolate mofetil, interferon beta-1a, interferon beta-lb, glatiramer acetate, mitoxantrone hydrochloride, and/or other biologics like anti-TNF. The domain antibodies also may be administered in combination with one or more of the following agents to regulate an immune response: CTLA4, soluble gp39 (also known as CD40 ligand (CD40L), CD154, T-BAM, TRAP), soluble CD29, soluble CD40, soluble CD80, soluble CD86, soluble CD56, soluble Thy-1, soluble CD3, soluble TCR, soluble VLA-4, soluble VCAM-1, soluble LECAM-1, soluble ELAM-1, soluble CD44, antibodies reactive with gp39, antibodies reactive with CD40, antibodies reactive with B7, antibodies reactive with CD28, antibodies reactive with LFA-1, antibodies reactive with LFA-2, antibodies reactive with IL-2, antibodies reactive with IL-12, antibodies reactive with IFN-gamma, antibodies reactive with CD2, antibodies reactive with CD48, antibodies reactive with any ICAM (e.g., ICAM-2), antibodies reactive with CTLA4, antibodies reactive with Thy-1, antibodies reactive with CD56, antibodies reactive with CD3, antibodies reactive with CD29, antibodies reactive with TCR, antibodies reactive with VLA-4, antibodies reactive with VCAM-1, antibodies reactive with LECAM-1, antibodies reactive with ELAM-1, antibodies reactive with CD44, monoclonal antibodies to leukocyte receptors, e.g., MHC, CD2, CD3, CD4, CD11a/CD18, CD7, CD25, CD 27, B7, CD40, CD45, CD58, CD 137, ICOS, CD150 (SLAM), OX40, 4-1BB or their ligands. The determination of the optimal combination and dosages can be determined and optimized using methods well known in the art.

Where domain antibodies of the invention are administered "in combination with" another immunosuppressive/immunomodulatory or anti-inflammatory agent or therapy, e.g., as specified above, the administration may be made concomitantly or in sequence. When the dAbs are administered concomitantly with another agent, such as an agent specified above, the dAb and agent may administered in the same pharmaceutical composition.

In an embodiment, a domain antibody is provided for the preparation of a medicament for the treatment of a patient, wherein the patient is in need of a CD28-binding domain antibody. In one embodiment, the patient is afflicted with an immune disease.

In one aspect, the immune disease is an autoimmune disease. An autoimmune disease includes, but is not limited to, Addison's disease, allergy, allergic rhinitis, ankylosing spondylitis, asthma, atherosclerosis, autoimmune diseases of the ear,

autoimmune diseases of the eye, autoimmune atrophic gastritis, autoimmune hepatitis, autoimmune hymolytic anemia, autoimmune parotitis, autoimmune uveitis, celiac disease, primary biliary cirrhosis, benign lymphocytic aniitis, COPD, colitis, coronary heart disease, Crohn's disease, diabetes (Type I), depression, diabetes, including Type 1 and/or Type 2 diabetes, epididymitis, glomerulonephritis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hemolytic anemia, idiopathic thrombocytopenic purpura, inflammatory bowel disease (IBD), immune response to recombinant drug products, e.g., factor VII in hemophilia, juvenile idiopathic arthritis, systemic lupus erythematosus, lupus nephritis, male infertility, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, oncology, osteoarthritis, pain, primary myxedema, pemphigus, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, reactive arthritis, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, spondyloarthropathies, sympathetic ophthalmia, T-cell lymphoma, T-cell acute lymphoblastic leukemia, testicular antiocentric T-cell lymphoma, thyroiditis, transplant rejection, ulcerative colitis, autoimmune uveitis, and vasculitis. Autoimmune diseases include, but are not limited to, conditions in which the tissue affected is the primary target, and in some cases, the secondary target. Such conditions include, but are not limited to, AIDS, atopic allergy, bronchial asthma, eczema, leprosy, schizophrenia, inherited depression, transplantation of tissues and organs, chronic fatigue syndrome, Alzheimer's disease, Parkinson's disease, myocardial infarction, stroke, autism, epilepsy, Arthus's phenomenon, anaphylaxis, and alcohol and drug addiction.

In another aspect, the immune disease is a graft-related disease, such as allograft rejection, xenograft rejection graft versus host disease (GVHD), acute transplantation rejection, and chronic transplantation rejection.

Included is a dAb that has at least three characteristics selected from the group consisting of:

a) prevents CD80 and CD86 binding to CD28,
b) does not agonize CD28 signaling in combination with T cell receptor signaling,
c) has a Kd of about 50 nM to about 1 pM for binding to CD28,
d) has a tα half-life of about 15 seconds to about 12 hours.
e) has a tβ half-life of about 12 hours to about 336 hours,
f) binds a MYPPPY sequence, and

g) a CDR1 sequence selected from the group consisting of SEQ ID NO:484, SEQ ID NO:487, SEQ ID NO:490, SEQ ID NO:493, SEQ ID NO:496, SEQ ID NO:499, SEQ ID NO:502, SEQ ID NO:505, SEQ ID NO:508, SEQ ID NO:511, SEQ ID NO:514, SEQ ID NO:517, SEQ ID NO:520, SEQ ID NO:523, SEQ ID NO:526, SEQ ID NO:529 and SEQ ID NO:636; a CDR2 sequence selected from the group consisting of SEQ ID NO:485, SEQ ID NO:488, SEQ ID NO:491, SEQ ID NO:494, SEQ ID NO:497, SEQ ID NO:500, SEQ ID NO:503, SEQ ID NO:506, SEQ ID NO:509, SEQ ID NO:512, SEQ ID NO:515, SEQ ID NO:518, SEQ ID NO:521, SEQ ID NO:524, SEQ ID NO:527, SEQ ID NO:530 and SEQ ID NO:637; and a CDR3 sequence selected from the group consisting of SEQ ID NO:486, SEQ ID NO:489, SEQ ID NO:492, SEQ ID NO:495, SEQ ID NO:498, SEQ ID NO:501, SEQ ID NO:504, SEQ ID NO:507, SEQ ID NO:510, SEQ ID NO:513, SEQ ID NO:516, SEQ ID NO:519, SEQ ID NO:522, SEQ ID NO:525, SEQ ID NO:528, SEQ ID NO:531and SEQ ID NO:638.

Also included is a nucleic acid encoding the dAbs disclosed herein.

Included is method of antagonizing CD28, comprising administering an effective amount of a dAb disclosed herein to an individual. Also included is a method of antagonizing the binding of CD28 comprising administering an effective amount of the dAb disclosed herein to an individual, wherein the dAb antagonizes the binding of CD28 to CD80 and/or CD86 in the individual.

Further included is a method of treating, alleviating, or preventing a symptom of an immune diease, such as an autoimmune disease or a graft-related disease, comprising administering an effective amount of a dAb disclosed herein to an individual having or at risk of having an immune disease. Included is a method of treating, alleviating, or preventing an immune disease, comprising administering an effective amount of a dAb disclosed herein to an individual having or at risk of having an immune disease.

Included herein is a pharmaceutical composition comprising a therapeutically-effective amount of a dAb disclosed herein and a pharmaceutically acceptable carrier.

Included is the use of a dAb disclosed herein for preparing a medicament for treating or preventing an immune disease in a patient in need thereof. Also included is the use of a dAb disclosed herein for preparing a medicament for treating or preventing a symptom of an immune disease in a patient in need thereof. Further included herein is

the use of a dAb disclosed herein for preparing a medicament for alleviating at least one symptom of an immune disease in a patient in need thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1, comprising FIGS. 1A and 1B, is a series of images depicting that anti-human CD28 domain antibodies set forth herein do not exhibit agonist activity. FIG. 1A illustrates that increasing concentrations of various dAbs do not activate CD28, while an anti-CD3 antibody (OKT3) control, added to PBMC, demonstrated activation of CD28. Domain antibodies (dAbs) and antibody were added to a 96-well plate that was seeded with PBMC isolated from whole blood of normal donors. FIG. 1B illustrates that dAbs, anti-CD28 (9.3), anti-CD3 (OKT3), or isotype control fixed to a 96-well round-bottom plate did not exhibit agonist activity in PBMC added to the wells.

FIG. 2 is a graphic depicting that anti-human CD28 domain antibodies do not exhibit co-agonist activity when added to 96-well flat-bottom plates coated with anti-CD3 (G19-4, 10 μg/ml in PBS). Each dAb was added to the well at a final concentration of 30 μg/ml along with purified T cells. As a positive control, anti-CD28 (mAb 9.3), at a final concentration of 1 μg/ml, was added in place of the dAb.

FIG. 3 is a graph depicting the *in vivo* inhibition of T cell proliferation by a domain antibody as set forth herein.

FIG. 4, comprising FIG.s 4A and 4B, is a series of images depicting the results of a nine-day receptor occupancy study, using dAb 1m-74-15-40L. FIG. 4A illustrates the receptor occupancy with intraperitoneal dosing of the dAb. FIG. 4B illustrates the receptor occupancy with subcutaneous dosing of the dAb.

FIG. 5 depicts the plasma concentration of dAbs 1h-99-2P40-branched and 1h-99-2P40-linear over time in a Cynomolgus monkey study.

FIG. 6 shows ELISAs of the binding to recombinant human CD28/Fc Chimera and Fc control coated plates of monoclonal phage displaying domain antibody clones.

FIG. 7 shows ELISAs of soluble monoclonal domain antibodies binding to recombinant human CD28/Fc Chimera and Fc control coated plates.

FIG. 8 shows BIAcore traces of dAb clones binding to a CM5 chip coated with 12500 units CD28-Fc.

FIG. 9A and FIG. 9B show the ability of domain antibody clones to inhibit the activity of CD28 in duplicate cell based "*in vitro*" assays. In the assays, human CD4 positive T cells are stimulated with anti-CD3 plus transfected CHO cells expressing either CD80 or CD86.

FIG 10 shows that anti-CD28 domain antibodies lack agonist activity. In FIG. 10A, PBMC were exposed to the anti-CD28 domain antibody 239-891-D70C or the mitogenic anti-CD28 antibody 5.11A1. Cell proliferation was measured by ^{3}[H]-thymidine incorporation on day 3, as shown in FIG. 10A, and IL-2 production was measured, as shown in FIG. 10B.

DETAILED DESCRIPTION

The present disclosure provides domain antibodies to antagonize CD28 activity. The domain antibodies may be linked to polymers to improve pharmacokinietic properties, such as stability and half-life. Included herein are compositions and methods for the attachment of polymer molecules (e.g., polyethylene glycol; PEG) to proteins to modulate the pharmacokinetic properties of the modified proteins. For example, PEG modification of proteins has been shown to alter the *in vivo* circulating half-life, antigenicity, solubility, and resistance to proteolysis of the protein (Abuchowski et al. (1977) *J. Biol. Chem.*, 252: 3578; Nucci et al. (1991) *Adv. Drug Delivery Reviews* 6: 133; Francis et al., *Pharmaceutical Biotechnology* Vol. 3 (Borchardt, R. T. ed.); and Stability of Protein Pharmaceuticals: *in vivo* Pathways of Degradation and Strategies for Protein Stabilization 1991 pp235-263, Plenum, NY).

1. Definitions and Acronyms

1.1. Definitions

In accordance with this detailed description, the following abbreviations and definitions apply. It must be noted that as used herein, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an antibody" includes a plurality of such antibodies and reference to "the dosage" includes reference to one or more dosages and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art. Unless

otherwise stated, all ranges described herein are inclusive of the specific endpoints. The following terms are provided below.

As used herein, the term "human" when applied to a domain antibody or to an immunoglobulin variable domain means that the polypeptide has a sequence derived from a human immunoglobulin. A sequence is "derived from" a human immunoglobulin coding sequence when the sequence is either: a) isolated from a human individual or from cells or a cell line from a human individual; b) isolated from a library of cloned human antibody gene sequences (or a library of human antibody V domain sequences); or c) when a cloned human antibody gene sequence (or a cloned human V region sequence (including, e.g., a germline V gene segment)) was used to generate one or more diversified sequences that were then selected for binding to a desired target antigen.

At a minimum, a human domain antibody has at least 70% identical, at least 75% identical, at least 80% identical, at least 85% amino acid identity (including, for example, 87%, 90%, 93%, 95%, 97%, 99%, or higher identity) to a naturally-occurring human immunoglobulin variable domain sequence, e.g., a naturally-occurring human immunoglobulin variable domain sequence disclosed in Kabat ("Sequences of Proteins of Immunological Interest", US Department of Health and Human Services 1991).

As used herein, the term "domain" refers to a folded protein structure which retains its tertiary structure independently of the rest of the protein. Generally, domains are responsible for discrete functional properties of proteins, and in many cases may be added, removed, or transferred to other proteins without loss of function of the remainder of the protein and/or of the domain.

By "domain antibody" is meant a folded polypeptide domain which comprises a sequence characteristic of immunoglobulin variable domains and which specifically binds an antigen (e.g., dissociation constant of 500 nM or less). A "domain antibody" therefore includes complete antibody variable domains as well as modified variable domains, for example in which one or more loops have been replaced by sequences which are not characteristic of antibody variable domains, or antibody variable domains which have been truncated or comprise N- or C-terminal extensions, as well as folded fragments of variable domains which retain a dissociation constant of 500 nM or less (e.g., 450 nM or less, 400 nM or less, 350 nM or less, 300 nM or less, 250 nM or less, 200 nM or less, 150 nM or less, 100 nM or less) and the target antigen specificity of the

full-length domain. Where necessary or in case of any doubt, the numbering convention and boundaries set forth by Kabat et al. (Kabat et al. (1991) *Sequences of Immunological Interest,* 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.) are applicable to immunoglobulin variable and constant domains referred to herein.

A "dAb" is used interchangeably with "domain antibody" herein.

A domain antibody, as used herein, refers to a mammalian immunoglobulin polypeptide, including human, but also includes rodent (for example, as disclosed in WO00/29004, the contents of which are incorporated herein in their entirety) or camelid V_{HH} dAbs. Camelid dAbs are antibody single variable domain polypeptides which are derived from species including camel, llama, alpaca, dromedary, and guanaco, and comprise heavy chain antibodies naturally devoid of light chain: V_{HH}. V_{HH} molecules are about 10X smaller than IgG molecules, and as single polypeptides, they are very stable, resisting extreme pH and temperature conditions.

Camelid antibodies are described in, for example, U.S. Pat. Nos. 5,759,808; 5,800,988; 5,840,526; 5,874,541; 6,005,079; and 6,015,695, the contents of each of which are incorporated herein in their entirety. Humanized camelid V_{HH} polypeptides are taught, for example in WO04/041862, the teachings of which are incorporated herein in their entirety. It will be understood by one of skill in the art that naturally occurring camelid antibody single variable domain polypeptides may be modified according to the teachings of WO04/041862 (e.g., amino acid substitutions at positions 45 and 103) to generate humanized camelid V_{HH} polypeptides. Also included herein are antibody single variable domain polypeptides which are nurse shark V_{HH}. Nurse Shark V_{HH} dAbs are described, for example, in Greenberg et al. (1995) *Nature* 374: 168-173 and U.S. Publication No. 20050043519.

As used herein, the phrase "sequence characteristic of immunoglobulin variable domains" refers to an amino acid sequence that is identical, over 20 or more, 25 or more, 30 or more, 35 or more, 40 or more, 45 or more, or even 50 or more contiguous amino acids, to a sequence comprised by an immunoglobulin variable domain sequence.

Sequences similar or identical (e.g., at least about 70% sequence identity) to the sequences disclosed herein are also included herein. In some embodiments, the sequence identity at the amino acid level can be about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher. At the nucleic acid level, the

sequence identity can be about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher. Alternatively, substantial identity exists when the nucleic acid segments will hybridize under selective hybridization conditions (e.g., very high stringency hybridization conditions), to the complement of the strand. The nucleic acids may be present in whole cells, in a cell lysate, or in a partially purified or substantially pure form.

As used herein, the term "identity" refer to the degree with which two nucleotide or amino acid sequences structurally resemble each other. As used herein, sequence "similarity" is a measure of the degree to which amino acid sequences share similar amino acid residues at corresponding positions in an alignment of the sequences. Amino acids are similar to each other where their side chains are similar. Specifically, "similarity" encompasses amino acids that are conservative substitutes for each other. A "conservative" substitution is any substitution that has a positive score in the blosum62 substitution matrix (Hentikoff and Hentikoff (1992) *Proc. Natl. Acad. Sci. USA* 89: 10915-10919). By the statement "sequence A is n% similar to sequence B" is meant that n% of the positions of an optimal global alignment between sequences A and B consists of identical amino acids or conservative substitutions. As used herein, two sequences are "similar" to each other, or share a "percent identity", when aligned using either the Needleman-Wunsch algorithm or the "BLAST 2 sequences" algorithm described by Tatusova & Madden (1999) *FEMS Microbiol Lett.* 174: 247-250. Where amino acid sequences are aligned using the "BLAST 2 sequences algorithm," the Blosum 62 matrix is the default matrix. Optimal global alignments can be performed using the following parameters in the Needleman-Wunsch alignment algorithm:

For polypeptides:

Substitution matrix: blosum62.

Gap scoring function: -A -B*LG, where A=11 (the gap penalty), B=1 (the gap length penalty) and LG is the length of the gap.

For nucleotide sequences:

Substitution matrix: 10 for matches, 0 for mismatches.

Gap scoring function: -A -B*LG where A=50 (the gap penalty), B=3 (the gap length penalty) and LG is the length of the gap.

Using the software AlignX, a component of Vector NTI Suite 8.0 (InforMax, Inc.), the alignment was created using the Clustal W algorithm (1994) *Nucleic Acid Research,* 22 (22): 4673-4680. In using this method, a crude similarity between all pairs of sequences is calculated, called a "Parities alignment." These scores are then used to calculate a "guide tree" or dendrogram, which tells the multiple alignment stage the order in which to align the sequences for the final multiple alignment. Having calculated the dendrogram, the sequences are aligned in larger and larger groups until the entire sequences are incorporated in the final alignment.

Alternatively, calculations of identity of amino acid and nucleic acid sequences are determined herein using the software AlignX, with the following parameters:

Use FAST Algorithm:	OFF
K-tuple size:	1
Number of best diagonals:	5
Window Size:	5
Gap penalty:	3
Gap opening penalty:	10
Gap extension penalty:	0.1

Multiple Alignment Settings for AlignX were set as follows:

Gap opening penalty:	10
Gap extension penalty:	0.05
Gap separation penalty range:	8
No end gap separation penalty:	Unselected
% identity for alignment delay:	40
Residue specific gaps off:	Unselected
Hydrophilic residue gap off:	Unselected
Transition weighting:	0

Typical conservative substitutions are exchanges among Met, Val, Leu, and Ile; among Ser and Thr; among the residues Asp, Glu, and Asn; among the residues Gln, Lys, and Arg; or aromatic residues Phe and Tyr.

As used herein, the term "epitope" refers to a unit of structure conventionally bound by an immunoglobulin V_H/V_L pair. Epitopes define the minimum binding site for an antibody, and thus represent the target of specificity of an antibody. In the case of a domain antibody, an epitope represents the unit of structure bound by a domain antibody in isolation. That is, the binding site is provided by one, single immunoglobulin variable domain. Epitopes can be linear or conformational, and can be as small as three amino acids.

As used herein, the term "extended release", or the equivalent terms "controlled release" or "slow release", refer to drug formulations that release active drug, such as a polypeptide drug, over a period of time following administration to an individual. Extended release of polypeptide drugs, which can occur over a range of desired times, e.g., minutes, hours, days, weeks, or longer, depending upon the drug formulation, is in contrast to standard formulations in which substantially the entire dosage unit is available for immediate absorption or immediate distribution via the bloodstream. Extended release formulations may result in a level of circulating drug from a single administration that is sustained, for example, for 8 hours or more, 12 hours or more, 24 hours or more, 36 hours or more, 48 hours or more, 60 hours or more, 72 hours or more 84 hours or more, 96 hours or more, or even, for example, for 1 week or 2 weeks or more, for example, 1 month or more.

As used herein, "CD28 activity" is an activity involving or resulting from the binding of CD80, CD86 and/or another ligand to CD28, and includes, but is not limited to, activation of CD28-mediated cell signaling. CD28 activity also includes the induction of T cell proliferation and the induction of cytokine secretion, e.g., interleukin 2 (IL-2), by T cells.

As used herein, the term "does not substantially agonize" means that a given agent, e.g., a domain antibody, does not substantially activate one or more of the CD28 activities as the term "activate" is defined herein. Specifically, an agent that "does not substantially agonize" means that the agent does not activate more than 20% of the activity which is activated by CD80 and/or CD86 binding to CD28, and in an aspect, the

agent does not activate more than about 10%, 8%, 5%, 3%, or 2% or less, including zero activation, of the activity which is activated by CD80 and/or CD86 binding to CD28. By way of a non-limiting example, a domain antibody set forth herein that does not substantially agonize CD28 activity does not agonize CD28 activity more than 5% of the activity obtained upon agonism of CD28 activity by anti-CD28 mAb 9.3 (Gibson, et al. (1996) *JBC*, 271: 7079-7083) under otherwise identical assay conditions.

As used herein, the terms "inhibit," "inhibits" and "inhibited" refer to a decrease in a given measurable activity (e.g., binding activity) by at least 10% relative to a reference. Where inhibition is desired, such inhibition is at least about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, up to and including 100%, i.e., complete inhibition or absence of the given activity. Inhibition of CD28 binding to CD80 or CD86 can be measured as described in the working examples herein. As used herein, the term "substantially inhibits" refers to a decrease in a given measurable activity (e.g., the binding of CD28 to CD80 or CD86) by at least 50% relative to a reference. For example, "substantially inhibits" refers to a decrease in a given measurable activity of at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, and up to and including 100% relative to a reference. As used herein, "inhibits the binding", with reference to the binding of a domain antibody binding to CD28, or CD80 binding to CD28, or CD86 binding to CD28, refers to a decrease in binding by at least 10% relative to a reference. "Inhibits the binding" refers to a decrease in binding of at least about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, up to and including 100%.

As used herein, the terms "activate," "activates" and "activated" refer to an increase in a given measurable activity by at least 5% relative to a reference, for example, at least 10%, 25%, 50%, 75%, or even 100%, or more.

As used herein, the term "CD28 antagonist" refers to an agent that inhibits at least one activity mediated by CD28, by inhibiting the binding of CD80 and/or CD86 to CD28. A CD28 activity is "antagonized" if the activity is reduced by at least 10%, and in an exemplary embodiment, at least about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 97%, or even 100% (i.e., no activity) in the presence, relative to the absence of an antagonist. In an exemplary embodiment, a CD28 antagonist as the term is used herein comprises a domain antibody that binds monovalently to CD28. By way of a non-limiting example, a CD28 antagonist as set forth herein is an agent that inhibits some or

all CD28 activity, while at the same time, the agent does not substantially agonize CD28 activity in combination with T cell receptor signaling.

As used herein, the term "preferentially inhibits" as used in a phrase such as "wherein a domain antibody preferentially inhibits the binding to CD28 by CD86 relative to the binding to CD28 by CD80", means that the domain antibody effects a higher amount of inhibition of CD86 binding to CD28 as defined above, relative to the amount of inhibition of CD80 binding to CD28 as defined above.

As used herein, the term "CD28 agonist" refers to an agent that activates at least one activity mediated by CD28, either alone or when combined with another co-stimulus, relative to a reference. An activity is "agonized" if the activity is increased by at least about 10%, e.g., 50%, in the presence, relative to the absence of an agonist.

As used herein, the inhibiting "CTLA4 activity" includes, but is not limited to, inhibition of T cell function. Such functions include, among others, T cell receptor mediated signaling, T cell proliferation, and induction of cytokine secretion.

As used herein, "immune disease" refers to any disease which is associated with the development of an immune reaction in an individual, including a cellular and/or a humeral immune reaction. Examples of immune diseases include, but are not limited to, inflammation, allergy, autoimmune diseases, and graft-related diseases.

As used herein, "autoimmune disease" refers to disease conditions and states wherein the immune response of an individual is directed against the individual's own constituents, resulting in an undesirable and often debilitating condition. As used herein, "autoimmune disease" is intended to further include autoimmune conditions, syndromes, and the like. Autoimmune diseases include, but are not limited to, Addison's disease, allergy, allergic rhinitis, ankylosing spondylitis, asthma, atherosclerosis, autoimmune diseases of the ear, autoimmune diseases of the eye, autoimmune atrophic gastritis, autoimmune hepatitis, autoimmune hymolytic anemia, autoimmune parotitis, autoimmune uveitis, celiac disease, primary biliary cirrhosis, benign lymphocytic aniitis, COPD, colitis, coronary heart disease, Crohn's disease, diabetes (Type I), depression, diabetes, including Type 1 and/or Type 2 diabetes, epididymitis, glomerulonephritis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hemolytic anemia, idiopathic thrombocytopenic purpura, inflammatory bowel disease (IBD), immune response to recombinant drug products, e.g., factor VII in

hemophilia, juvenile idiopathic arthritis, systemic lupus erythematosus, lupus nephritis, male infertility, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, oncology, osteoarthritis, pain, primary myxedema, pemphigus, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, reactive arthritis, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, spondyloarthropathies, sympathetic ophthalmia, T-cell lymphoma, T-cell acute lymphoblastic leukemia, testicular antiocentric T-cell lymphoma, thyroiditis, transplant rejection, ulcerative colitis, autoimmune uveitis, and vasculitis. Autoimmune diseases include, but are not limited to, conditions in which the tissue affected is the primary target, and in some cases, the secondary target. Such conditions include, but are not limited to, AIDS, atopic allergy, bronchial asthma, eczema, leprosy, schizophrenia, inherited depression, transplantation of tissues and organs, chronic fatigue syndrome, Alzheimer's disease, Parkinson's disease, myocardial infarction, stroke, autism, epilepsy, Arthus's phenomenon, anaphylaxis, and alcohol and drug addiction.

As used herein, the term "antibody polypeptide" refers to a polypeptide which either is an antibody or is a part of an antibody, modified or unmodified, which retains the ability to specifically bind antigen. Thus, the term antibody polypeptide includes an antigen-binding heavy chain, light chain, heavy chain-light chain dimer, Fab fragment, $F(ab')_2$ fragment, dAb, or an Fv fragment, including a single chain Fv (scFv). The phrase "antibody polypeptide" is intended to encompass recombinant fusion polypeptides that comprise an antibody polypeptide sequence that retains the ability to specifically bind antigen in the context of the fusion.

As used herein, the term "monovalent" means that a given domain antibody can bind only a single molecule of its target. Naturally-occurring antibodies are generally divalent, in that they have two functional antigen-binding loops, each comprising a VH and a VL domain. Where steric hindrance is not an issue, a divalent antibody can bind two separate molecules of the same antigen. In contrast, a "monovalent" antibody has the capacity to bind only one such antigen molecule. As the term is used herein, a "monovalent" antibody can also comprise more than one antigen binding site, e.g., two antigen binding sites, but the binding sites must be for different antigens, such that the antibody can only bind one molecule of CD28 at a time. The antigen-binding domain of a monovalent antibody can comprise a V_H and a V_L domain, but in an aspect, comprises only a single immunoglobulin variable domain, i.e., a V_H or a V_L domain, that has the

capacity to bind CD28 without the need for a corresponding V_L or V_H domain, respectively. A monovalent antibody lacks the capacity to cross link molecules of a single antigen.

As used herein, the term "standard platelet aggregation assay" means the assay described in the section herein below, entitled "Platelet Aggregation Assay."

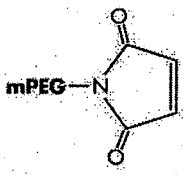
As used herein, the terms "V_H domain" and "V_L domain" refer to immunoglobulin variable regions as defined by Kabat et al. (Kabat et al. (1991) *Sequences of Immunological Interest,* 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.), which is incorporated herein by reference.

As used herein, "linked" refers to the attachment of a polymer moiety, such as PEG to an amino acid residue of a domain antibody. Attachment of a PEG polymer to an amino acid residue of a domain antibody, e.g., a domain antibody, is referred to as "PEGylation" and may be achieved using several PEG attachment moieties including, but not limited to N-hydroxylsuccinimide (NHS) active ester, succinimidyl propionate (SPA), maleimide (MAL), vinyl sulfone (VS), or thiol. A PEG polymer, or other polymer, can be linked to a domain antibody at either a predetermined position, or may be randomly linked to the domain antibody molecule. The PEG polymer may be linked to a domain antibody at a predetermined position. A PEG polymer may be linked to any residue in a domain antibody, however, it is preferable that the polymer is linked to either a lysine or cysteine, which is either naturally occurring in the domain antibody or which has been engineered into the domain antibody, for example, by mutagenesis of a naturally occurring residue in the domain antibody to either a cysteine or lysine. PEG-linkage can also be mediated through a peptide linker attached to a domain antibody. That is, the PEG moiety can be attached to a peptide linker fused to a domain antibody, where the linker provides the site, e.g., a free cysteine or lysine, for PEG attachment. As used herein, "linked" can also refer to the association of two or more domain antibodies, e.g., dAb monomers, to form a dimer, trimer, tetramer, or other multimer. Domain antibody monomers can be linked to form a multimer by several methods known in the art, including, but not limited to, expression of the domain antibody monomers as a fusion protein, linkage of two or more monomers via a peptide linker between monomers, or by chemically joining monomers after translation, either to each other directly, or through a linker by disulfide bonds, or by linkage to a di-, tri- or multivalent linking moiety (e.g., a multi-arm PEG). While dAb multimers are specifically contemplated herein, e.g., in the

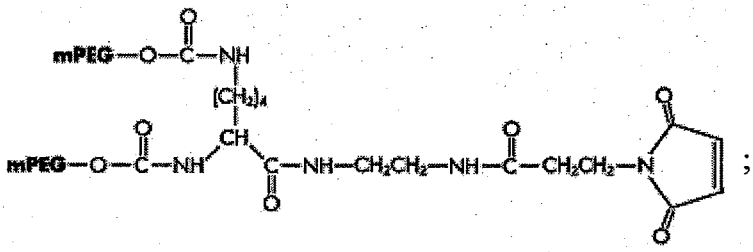
context of dual- or multi-specific domain antibody constructs, it is emphasized that for any given domain antibody construct, the construct should only be able to bind one molecule of CD28, i.e., the constructs should have only one CD28-binding element, and should not cross link CD28.

As used herein, "polymer" refers to a macromolecule made up of repeating monomeric units, and can refer to a synthetic or naturally occurring polymer such as an optionally substituted straight or branched chain polyalkylene, polyalkenylene, or polyoxyalkylene polymer or a branched or unbranched polysaccharide. A "polymer" as used herein, specifically refers to an optionally substituted or branched chain poly(ethylene glycol), poly(propylene glycol), or poly(vinyl alcohol) and derivatives thereof.

As used herein, "PEG" or "PEG polymer" refers to polyethylene glycol, and more specifically can refer to a derivatized form of PEG, including, but not limited to N-hydroxylsuccinimide (NHS) active esters of PEG such as succinimidyl propionate, benzotriazole active esters, PEG derivatized with maleimide, vinyl sulfones, or thiol groups. For example, PEG formulations can include PEG-O-$CH_2CH_2CH_2$-CO_2-NHS; PEG-O-CH_2-NHS; PEG-O-CH_2CH_2-CO_2-NHS; PEG-S-CH_2CH_2-CO-NHS; PEG-O_2CNH-CH(R)-CO_2-NHS; PEG-NHCO-CH_2CH_2-CO-NHS; and PEG-O-CH_2-CO_2-NHS; where R is $(CH_2)_4$)$NHCO_2$(mPEG). PEG polymers set forth herein may be linear molecules, or may be branched wherein multiple PEG moieties are present in a single polymer. Some representative PEG conformations include, but are not limited to the following:

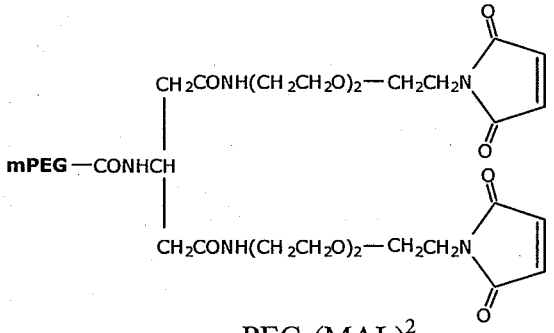


;



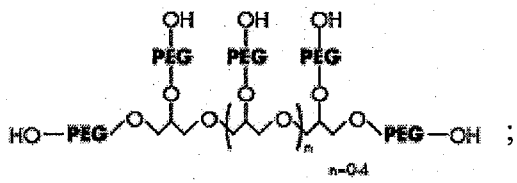
;

mPEG-MAL mPEG2-MAL



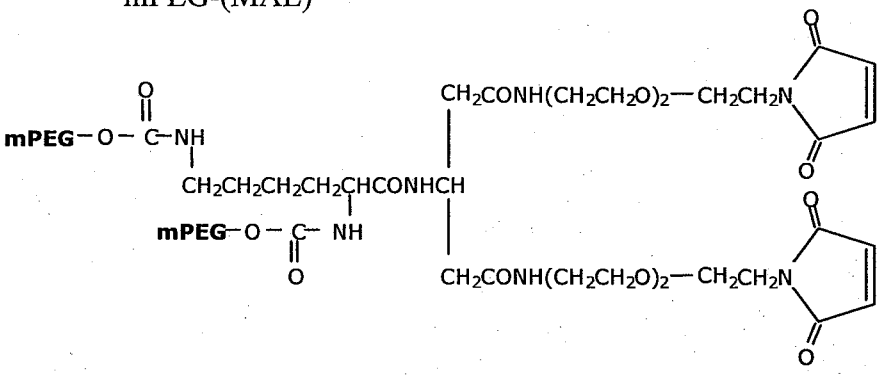
mPEG-(MAL)^2

;

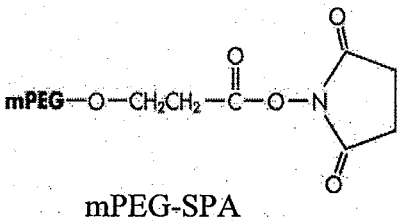


multi-arm PEG

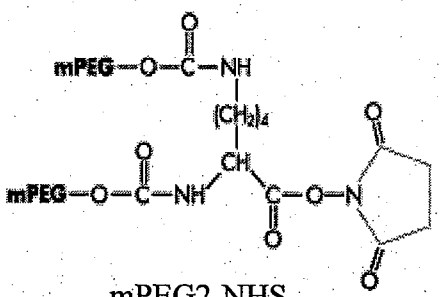
;



mPEG2-(MAL)^2



mPEG-SPA



mPEG2-NHS

As used herein, a "sulfhydryl-selective reagent" is a reagent which is useful for the attachment of a PEG polymer to a thiol-containing amino acid. Thiol groups on the amino acid residue cysteine are particularly useful for interaction with a sulfhydryl-selective reagent. Sulfhydryl-selective reagents which are useful for such attachment include, but are not limited to maleimide, vinyl sulfone, and thiol. The use of sulfhydryl-selective reagents for coupling to cysteine residues is known in the art and may be adapted as needed (*see, e.g.*, Zalipsky (1995) *Bioconjug. Chem.* 6: 150; Greenwald et al. (2000) *Crit. Rev. Ther. Drug Carrier Syst.* 17: 101; Herman et al. (1994) *Macromol. Chem. Phys.* 195: 203).

The attachment of PEG or another agent, e.g., HSA, to a domain antibody as described herein in an exemplary embodiment, will not impair the ability of the polypeptide to specifically bind CD28. That is, the PEG-linked domain antibody will retain its binding activity relative to a non-PEG-linked counterpart. As used herein, "retains activity" refers to a level of activity of a PEG-linked domain antibody which is at least 10% of the level of activity of a non-PEG-linked domain antibody, including at least about 20%, 30%, 40%, 50%, 60%, 70%, 80%, and up to 90%, including up to about 95%, 98%, and up to 100% of the activity of a non-PEG-linked domain antibody comprising the same antigen-binding domain or domains. More specifically, the activity of a PEG-linked domain antibody compared to a non-PEG linked domain antibody should be determined on an antibody polypeptide molar basis; that is equivalent numbers of moles of each of the PEG-linked and non-PEG-linked domain antibody should be used in each trial. In determining whether a particular PEG-linked domain antibody "retains activity", the activity of a PEG-linked domain antibody may be compared with the activity of the same domain antibody in the absence of PEG.

As used herein, the term "*in vivo* half-life" refers to the time taken for the serum concentration of a ligand (e.g., a domain antibody) to reduce by about 50%, *in vivo*, for example due to degradation of the ligand and/or clearance or sequestration of the ligand by natural mechanisms. The domain antibodies described herein can be stabilized *in vivo* and their half-life increased by binding to molecules, such as PEG, which resist degradation and/or clearance or sequestration. The half-life of a domain antibody is increased if its functional activity persists, *in vivo*, for a longer period than a similar antibody polypeptide which is not linked to a PEG polymer. Typically, the half-life of a PEGylated domain antibody is increased by at least about 10%, 20%, 30%, 40%, 50%, or more relative to a non-PEGylated domain antibody. Increases in the range of 2X, 3X, 4X, 5X, 10X, 20X, 30X, 40X, 50X, or more of the half-life are possible. Alternatively, or in addition, increases in the range of up to 30X, 40X, 50X, 60X, 70X, 80X, 90X, 100X, or 150X of the half-life are possible. As set forth herein, a PEG-linked domain antibody has a half-life of between 0.25 and 170 hours, including between 1 and 100 hours, further including between 30 and 100 hours, and still further including between 50 and 100 hours, and up to 170, 180, 190, and 200 hours or more.

As used herein, "resistant to degradation" or "resists degradation" with respect to a PEG or other polymer-linked domain antibody monomer or multimer means that the

PEG- or other polymer-linked domain antibody monomer or multimer is degraded by no more than about 10% when exposed to pepsin at pH 2.0 for 30 minutes and in an aspect, not degraded at all.

As used herein, "hydrodynamic size" refers to the apparent size of a molecule (e.g., a protein molecule) based on the diffusion of the molecule through an aqueous solution. The diffusion, or motion, of a protein through solution can be processed to derive an apparent size of the protein, where the size is given by the "Stokes radius" or "hydrodynamic radius" of the protein particle. The "hydrodynamic size" of a protein depends on both mass and shape (conformation), such that two proteins having the same molecular mass may have differing hydrodynamic sizes based on the overall conformation of the protein. Hydrodynamic size is measured, for example, by size exclusion chromatography. The hydrodynamic size of a PEG-linked antibody polypeptide, e.g., a domain antibody, can be in the range of about 24 kD to 500 kD; 30 to 500 kD; 40 to 500 kD; 50 to 500 kD; 100 to 500 kD; 150 to 500 kD; 200 to 500 kD; 250 to 500 kD; 300 to 500 kD; 350 to 500 kD; 400 to 500 kD, and 450 to 500 kD. In an aspect, the hydrodynamic size of a PEGylated domain antibody is about 30 to 40 kD; 70 to 80 kD, or 200 to 300 kD. Where a domain antibody is desired for use in imaging applications, the domain antibody should have a hydrodynamic size of between about 50 and 100 kD. Alternatively, where a domain antibody is desired for therapeutic applications, the domain antibody preparation should have a hydrodynamic size of greater than about 200 kD.

As used herein, the term "IC_{50}" refers to the concentration of an inhibitor necessary to inhibit a given activity by about 50%. IC_{50} is determined by assaying a given activity, e.g., binding of CD28 to CD80 or CD86, in the presence of varying amounts of the inhibitor (e.g., domain antibody), and plotting the inhibitor concentration versus the activity being targeted. Binding of CD28 to CD80 or CD86 is measured herein by the method described the working examples. Alternatively, surface plasmon resonance (SPR) can be used.

As used herein, the term "EC_{50}" refers to the concentration of compound or domain antibody that provokes a response in a subject, wherein the response is halfway between the baseline and the maximum response. The baseline and maximum responses of a subject, with respect to a compound or domain antibody, can be determined by any technique known in the art.

As used herein, the term "fused to a domain antibody" generally means that a polypeptide is fused to a given antibody through use of recombinant DNA techniques, though fusion may occur chemically at the protein level. Thus, an antibody "fused to" another polypeptide, e.g., to another antibody of different binding specificity, does not exist in nature and is generated through recombinant means. The term "fused to a domain antibody" also encompasses the linkage of a polypeptide to a given domain antibody through, for example, disulfide or other chemical linkages, where the fused polypeptide is not naturally found fused to the domain antibody. Recombinant and chemical methods of fusing a polypeptide to another polypeptide, e.g., to an antibody, are well known in the art.

As used herein, the term "Fc domain" refers to the constant region antibody sequences comprising CH2 and CH3 constant domains as delimited according to Kabat et al., *supra*. The Fc portion of the heavy chain polypeptide has the ability to self-associate, a function which facilitates the formation of divalent antibodies. The term "lacks an Fc domain" means that a given domain antibody lacks at least the portion of an immunoglobulin Fc domain (as such domains are defined according to Kabat et al., 1991, *Sequences of Immunological Interest,* 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.) sufficient to mediate the dimerization of Fc-containing domain antibodies. Dimerization of Fc-containing domain antibodies is measured, for example, by chromatographic methods or by surface plasmon resonance. A domain antibody lacking an Fc domain avoids Fc-platelet interactions and therefore avoids induction of platelet aggregation.

As used herein "treat", "reduce", "prevent", or "alleviate" as it relates to a symptom of disease refer to a decrease of a symptom by at least 10% based on a clinically measurable parameter, or by at least one point on a clinically-accepted scale of disease or symptom severity. As used herein, the term "symptom(s) of systemic lupus erythematosus" refers to any of the clinically relevant symptoms of SLE known to those of skill in the art. Non-limiting examples include the accumulation of IgG autoantibodies (e.g., against nuclear antigens such as chromatin, snRNPs (especially U1, Sm, Ro/SSA and La/SSB), phospholipids and cell surface molecules), hemolytic anemia, thrombocytopenia, leukopenia, glomerulonephritis, vasculitis, arthritis, and serositis). A reduction in such a symptom is a reduction by at least 10% in a clinically measurable parameter, or by at least one point on a clinically-accepted scale of disease severity.

As used herein, the phrase "specifically binds" refers to the binding of an antigen by a domain antibody with a dissociation constant (K_d) of 1 μM or lower as measured by surface plasmon resonance analysis using, for example, a BIAcore™ surface plasmon resonance system and BIAcore™ kinetic evaluation software (e.g., version 2.1). The affinity or K_d for a specific binding interaction, in an aspect, is about 500 nM or lower, and in another aspect, about 300 nM or lower.

As used herein, a "generic ligand" is a ligand that binds a substantial proportion of functional members in a given repertoire, e.g., in a phage display library. Thus, the same generic ligand can bind many members of the repertoire regardless of their target ligand specificities. In general, the presence of a functional generic ligand binding site indicates that the repertoire member is expressed and folded correctly. Thus, binding of the generic ligand to its binding site provides a method for preselecting functional polypeptides from a repertoire of polypeptides. Generic ligands include, for example, Protein A, Protein G and Protein L.

As used herein, the term "universal framework" refers to a single antibody framework sequence corresponding to the regions of an antibody conserved in sequence as defined by Kabat (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.) or corresponding to the human germline immunoglobulin repertoire or structure as defined by Chothia and Lesk, (1987) J. Mol. Biol. 196: 910-917. The use of a single framework, or a set of such frameworks, which has been found to permit the derivation of virtually any binding specificity though variation in the hypervariable regions alone, is included herein.

The term "about" will be understood by persons of ordinary skill in the art and will vary to some extent on the context in which it is used. Generally, about encompasses a range of values that are plus/minus 10% of a referenced value.

The term "corresponds to" as used herein with respect to protein or nucleic acid sequences and/or domains refer to an analogous sequence or structure on a separate protein. For example, a calcium-biding domain of mouse myosin "corresponds to" the calcium-binding domain of a human myosin.

1.2. Acronyms

The following is a list of terms and associated acronyms used herein and apply to the referenced terms, unless otherwise indicated with specific terms and acronyms.

Ab	antibody
AIDS	acquired immune deficiency syndrome
APC	antigen presenting cell
AUC	area under the curve
BSA	bovine serum albumin
cDNA	complementary DNA
CD80	B7-1 co-stimulatory molecule on APCs
CD86	B7-2 co-stimulatory molecule on APCs
CDR	complementarity determining region
CTLA-4	a/k/a/ CD152; a high affinity CD80/CD86 receptor on T cells
CRS	cytokine release syndrome
dAb	domain antibody
DC	dendritic cell
DNA	deoxyribonucleic acid
EDTA	ethylenediaminetetraacetic acid
ELISA	enzyme-linked immunosorbent assay
Fab	antigen binding region
Fc	antibody tail region
FCS	fetal calf serum
FW	framework
HPLC	high performance liquid chromatography
HSA	human serum albumin
IFN	interferon
IL	interleukin
kD	kiloDalton
K_d	dissociation constant
mAb	monoclonal antibody
MAL	maleimide
mg	milligram
ml	milliliter

MLR	mixed lymphocyte reaction
mM	millimolar
MoDC	monocyte-derived dendritic cells
MSA	mouse serum albumin
NHS	N-hydroxylsuccinimide
ng	nanogram
nM	nanomolar
pg	picogram
pM	picomolar
mRNA	messenger ribonucleic acid
PBMC	peripheral blood mononuclear cells
PCR	polymerase chain reaction
PDB	Protein Database Base
PEG	polyethyleneglycol
PK	pharmacokinetics
ppm	parts per million
RO	receptor occupancy
RT-PCR	reverse transcriptase polymerase chain reaction
SA	serum albumin
scFV	single chain variable fragment
SDS-PAGE	sodium dodecyl sulfate-polyacrylamide gel electrophoresis
SEC-MALLS	size-exclusion chromatography multi-angle laser light scattering
SPA	succinimidyl propionate
SPR	surface plasmon resonance
SRBC	sheep red blood cells
$t_{½}$	half life
TNF	tumor necrosis factor
t.u.	titer units
µg	microgram
µl	microliter
µM	micromolar
V_H	variable heavy-chain domain
V_L	variable light-chain domain
VS	vinyl sulfate

1X SSC 0.15 M NaCl, 0.015 M sodium citrate, pH 7.0

Domain antibodies are provided that are monovalent for binding to CD28. While not wishing to be bound by any particular theory, it is believed that monovalency for CD28 binding removes the possibility for cross-linking cell surface receptors that occurs with prior art antibodies. Thus, in one aspect, the domain antibodies disclosed herein not only inhibit or antagonize the binding of CD80 or CD86 to CD28, they do not substantially agonize CD28 activity.

In one aspect, the antibodies monovalent for CD28 binding are human domain antibodies. Human domain antibodies can be administered to human patients while largely avoiding the anti-antibody immune response often provoked by the administration of antibodies from other species, e.g., mouse. While murine antibodies can be "humanized" by grafting human constant domains onto the murine antigen-binding domains, human antibodies as disclosed herein are produced without the need for laborious and time-consuming genetic manipulation of a murine antibody sequence.

2. Monovalent Domain Antibodies

The heavy and light polypeptide chains of antibodies comprise variable (V) regions that directly participate in antigen interactions, and constant (C) regions that provide structural support and function in non-antigen-specific interactions with immune effectors. The antigen binding domain of a conventional antibody is comprised of two separate domains: a heavy chain variable domain (V_H) and a light chain variable domain (V_L, which can be either V_κ or V_λ). The antigen binding site itself is formed by six polypeptide loops: three from the V_H domain (H1, H2 and H3) and three from the V_L domain (L1, L2 and L3). *In vivo*, a diverse primary repertoire of V genes that encode the V_H and V_L domains is produced by the combinatorial rearrangement of gene segments. C regions include the light chain C regions (referred to as C_L regions) and the heavy chain C regions (referred to as C_H1, C_H2 and C_H3 regions). A naturally-occurring antibody generally comprises two antigen binding domains and is therefore divalent.

A number of smaller antigen binding fragments of naturally occurring antibodies have been identified following protease digestion. These include, for example, the "Fab fragment" (V_L-C_L/C_H1-V_H), "Fab' fragment" (a Fab with the heavy chain hinge region), and "F(ab')$_2$ fragment" (a dimer of Fab' fragments joined by the heavy chain hinge region). Recombinant methods have been used to generate such fragments and to

generate even smaller antigen-binding fragments, e.g., those referred to as "single chain Fv" (variable fragment) or "scFv," consisting of V_L and V_H joined by a peptide linker (V_L-linker-V_H). Fab fragments, Fab' fragments and scFv fragments are monovalent for antigen binding, as they each comprise only one antigen binding domain comprising one V_H/V_L dimer.

A domain antibody, or "dAb", binds antigen independently of other V domains; however, a domain antibody can be present in a homo- or heteromultimer with other V_H or V_L domains where the other domains are not required for antigen binding by the dAb, i.e., where the dAb binds antigen independently of the additional V_H or V_L domains. The preparation of domain antibodies is described and exemplified herein below.

Antibody single variable domains, for example, V_{HH}, are the smallest antigen-binding antibody unit known. For use in therapy, human antibodies are especially advantageous, primarily because they are not as likely to provoke an immune response when administered to a patient. Comparisons of camelid V_{HH} with the V_H domains of human antibodies reveals several key differences in the framework regions of the camelid V_{HH} domain corresponding to the V_H/V_L interface of the human V_H domains. Mutation of these residues of human V_H3 to more closely resemble the V_{HH} sequence (specifically Gly 44→Glu, Leu 45→Arg and Trp 47→Gly) has been performed to produce "camelized" human V_H domains that retain antigen binding activity (Davies & Riechmann (1994) *FEBS Lett.* 339: 285-290) yet have improved expression and solubility. (Variable domain amino acid numbering used herein is consistent with the Kabat numbering convention (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.)) WO 03/035694 (Muyldermans) reports that the Trp 103→Arg mutation improves the solubility of non-camelid V_H domains. Davies & Riechmann (1995) *Biotechnology* N.Y. 13: 475-479 also report production of a phage-displayed repertoire of camelized human V_H domains and selection of clones that bind hapten with affinities in the range of 100-400 nM, but clones selected for binding to protein antigen had weaker affinities.

Domain antibodies can be generated in several different ways. For example, the nucleic acid sequence encoding heavy and light chains of an antibody known to bind CD28 can be manipulated to generate a number of different domain antibodies that are monovalent for CD28 binding. Thus, given the sequences encoding the heavy and light chain polypeptides that constitute an antibody and standard molecular cloning

methodologies, one can generate monovalent antigen-binding polypeptide constructs such as Fab fragments, scFv, dAbs, or even bispecific antibodies (i.e., antibodies that comprise two different antigen-binding moieties and can therefore bind two separate antigens, and in an aspect, simultaneously) that are monovalent for CD28.

2.1. General Strategy and Methods for Design of Domain Antibodies

One means of generating domain antibodies specific for CD28 is to amplify and express the V_H and V_L regions of the heavy chain and light chain gene sequences isolated, for example, from a hybridoma (e.g., a mouse hybridoma) that expresses domain antibody. The boundaries of V_H and V_L domains are set out by Kabat et al. (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.). The information regarding the boundaries of the V_H and V_L domains of heavy and light chain genes is used to design PCR primers that amplify the V domain from a heavy or light chain coding sequence encoding an antibody known to bind CD28. The amplified V domains are inserted into a suitable expression vector, e.g., pHEN-1 (Hoogenboom et al. (1991) *Nucleic Acids Res.* 19: 4133-4137) and expressed, e.g., as a fusion of the V_H and V_L in a scFv or other suitable monovalent format. The resulting polypeptide is then screened for high affinity monovalent binding to CD28. In conjunction with the methods set forth herein, screening for binding is performed as known in the art or as described herein below.

Alternatively, library screening methods can be used to identify monovalent CD28-specific binding proteins. Phage display technology (see, e.g., Smith (1985) *Science* 228: 1315; Scott & Smith (1990) Science 249: 386; McCafferty et al. (1990) *Nature* 348: 552) provides an approach for the selection of domain antibodies which bind a desired target from among large, diverse repertoires of domain antibodies. These phage-antibody libraries can be grouped into two categories: natural libraries which use rearranged V genes harvested from human B cells (Marks et al. (1991) *J. Mol. Biol.*, 222: 581; Vaughan et al. (1996) *Nature Biotech.*, 14: 309) or synthetic libraries whereby germline V gene segments or other domain antibody coding sequences are "rearranged" *in vitro* (Hoogenboom & Winter (1992) *J. Mol. Biol.*, 227: 381; Nissim et al. (1994) *EMBO J.*, 13: 692; Griffiths et al. (1994) *EMBO J.*, 13: 3245; De Kruif et al. (1995) *J. Mol. Biol.*, 248: 97) or where synthetic CDRs are incorporated into a single rearranged V gene (Barbas et al. (1992) *Proc. Natl. Acad. Sci. USA*, 89: 4457). Methods involving

genetic display packages (e.g., phage display, polysome display) are well-suited for the selection of monovalent CD28-specific antibody constructs because they generally express only monovalent fragments, rather than whole, divalent antibodies, on the display packages. Methods for the preparation of phage display libraries displaying various antibody fragments are described in the preceding references. Such methods are also described, for example, in U.S. Patent No. 6,696,245, which is incorporated herein by reference. The methods described in the '245 patent generally involve the randomization of selected regions of immunoglobulin gene coding regions, in particular V_H and V_L coding regions, while leaving other regions non-randomized (see below). The '245 patent also describes the generation of scFv constructs comprising individually randomized V_H and V_L domains.

Analysis of the structures and sequences of antibodies has shown that five of the six antigen binding loops (H1, H2, L1, L2, L3) possess a limited number of main-chain conformations or canonical structures (Chothia and Lesk (1987) J. *Mol. Biol.* 196: 901; Chothia et al. (1989) *Nature* 342: 877). The main-chain conformations are determined by (i) the length of the antigen binding loop, and (ii) particular residues, or types of residue, at certain key positions in the antigen binding loop and the antibody framework. For example, analysis of the loop lengths and key residues has enabled the prediction of the main-chain conformations of H1, H2, L1, L2 and L3 encoded by the majority of human antibody sequences (Chothia et al. (1992) *J. Mol. Biol.* 227: 799; Tomlinson et al. (1995) *EMBO J.* 14: 4628; Williams et al. (1996) *J. Mol. Biol.* 264: 220). Although the H3 region is much more diverse in terms of sequence, length and structure (due to the use of D segments), it also forms a limited number of main-chain conformations for short loop lengths which depend on the length and the presence of particular residues, or types of residue, at key positions in the loop and the antibody framework (Martin et al. (1996) *J. Mol. Biol.* 263: 800; Shirai et al. (1996) *FEBS Letters* 399: 1.

While, in one approach, diversity can be added to synthetic repertoires at any site in the CDRs of the various antigen-binding loops, this approach results in a greater proportion of V domains that do not properly fold and therefore contribute to a lower proportion of molecules with the potential to bind antigen. An understanding of the residues contributing to the main chain conformation of the antigen-binding loops permits the identification of specific residues to diversify in a synthetic repertoire of V_H or V_L domains. That is, diversity is best introduced in residues that are not essential to

maintaining the main chain conformation. As an example, for the diversification of loop L2, the conventional approach would be to diversify all the residues in the corresponding CDR (CDR2) as defined by Kabat et al. (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.), some seven residues. However, for L2, it is known that positions 50 and 53 are diverse in naturally occurring antibodies and are observed to make contact with the antigen. One approach would be to diversify only those two residues in this loop. This represents a significant improvement in terms of the functional diversity required to create a range of antigen binding specificities.

Immunoglobulin polypeptide libraries can advantageously be designed to be based on predetermined variable domain main chain conformation. Such libraries may be constructed as described in International Patent Application WO 99/20749, the contents of which are incorporated herein by reference. Thus, in one aspect, a domain antibody comprises the amino acid sequence of a given human germline V region gene segment, e.g., V_H germline gene segment DP-47, or V_κ germline gene segment DPK9. Such variable region polypeptides can be used for the production of scFvs or Fabs, e.g., a scFv or Fab comprising (i) an antibody heavy chain variable domain (V_H), or antigen binding fragment thereof, which comprises the amino acid sequence of germline V_H segment DP-47 and (ii) an antibody light chain variable domain (V_L), or antigen binding fragment thereof, which comprises the amino acid sequence of germline V_κ segment DPK9. Diversification of sequences within the context of the selected heavy and light chain germline gene segments, e.g., DP-47, DPK 9, DP45, DP38, etc. can generate a repertoire of diverse immunoglobulin coding sequences. One approach to diversification is described below in the context of generating a library of diversified domain antibody or scFv sequences. These variable region polypeptides can also be expressed as domain antibodies and screened for high affinity binding to CD28. The repertoire can be cloned into or generated in a vector suitable for phage display, e.g., a lambda or filamentous bacteriophage display vector and is then screened for binding to a given target antigen, e.g., CD28.

3. Preparation of Domain Antibodies

A domain antibody is a folded polypeptide domain which comprises sequences characteristic of immunoglobulin variable domains and which specifically binds an

antigen (e.g., dissociation constant of 500 nM or less), and which binds antigen as a single variable domain; that is, there is one binding site provided by a domain antibody without any complementary variable domain. A domain antibody therefore includes complete antibody variable domains as well as modified variable domains, for example in which one or more loops have been replaced by sequences which are not characteristic of antibody variable domains or antibody variable domains which have been truncated or comprise N- or C-terminal extensions, as well as folded fragments of variable domains which retain a dissociation constant of about 500 nM less (e.g., about 450 nM or less, about 400 nM or less, about 350 nM or less, about 300 nM or less, about 250 nM or less, about 200 nM or less, about 150 nM or less, about 100 nM or less) and the target antigen specificity of the full-length domain. In an exemplary embodiment, an antibody single variable domain useful in the compositions and methods set forth herein is selected from the group of V_H and V_L, including V_{kappa} and V_{lambda}. In an exemplary embodiment, the domain antibodies of use herein are "human" as that term is defined herein.

3.1.1. Structure of Ligands

According to one aspect disclosed herein, two or more non-complementary epitope binding domains are linked so that they are in a closed conformation as herein defined. Advantageously, they may be further attached to a skeleton which may, as an alternative, or on addition to a linker described herein, facilitate the formation and/or maintenance of the closed conformation of the epitope binding sites with respect to one another. Alternatively, the domain antibodies disclosed herein may be constructed using scaffold or skeleton frameworks as discussed herein.

Ligand skeletons may be based on immunoglobulin molecules or may be non-immunoglobulin in origin as set forth elsewhere herein. Immunoglobulin skeletons as herein defined may include any one or more of those selected from the following: an immunoglobulin molecule comprising at least (i) the CL (kappa or lambda subclass) domain of an antibody; or (ii) the CH1 domain of an antibody heavy chain; an immunoglobulin molecule comprising the CH1 and CH2 domains of an antibody heavy chain; an immunoglobulin molecule comprising the CH1, CH2 and CH3 domains of an antibody heavy chain; or any of the subset (ii) in conjunction with the CL (kappa or lambda subclass) domain of an antibody. A hinge region domain may also be included. Such combinations of domains may, for example, mimic natural antibodies, such as IgG

or IgM, or fragments thereof, such as Fv, scFv, Fab, or $F(ab')_2$ molecules. Those skilled in the art will be aware that this list is not intended to be exhaustive.

Each epitope binding domain comprises a protein scaffold and one or more CDRs which are involved in the specific interaction of the domain with one or more epitopes. Advantageously, an epitope binding domain disclosed herein comprises three CDRs. Suitable protein scaffolds, in addition to those based on immunoglobulin domains, may also be based on protein scaffolds or skeletons other than immunoglobulin domains. For example natural bacterial receptors such as SpA have been used as scaffolds for the grafting of CDRs to generate ligands which bind specifically to one or more epitopes. Details of this procedure are described in US 5,831,012. Other suitable scaffolds include those based on fibronectin and affibodies (Affibody, Bromma, Sweden). Details of suitable procedures are described in WO 98/58965. Other suitable scaffolds include lipocallin and CTLA4, as described in van den Beuken *et al.*, (2001) *J. Mol. Biol.*310: 591-601, and scaffolds such as those described in WO 00/69907 (Medical Research Council), which are based for example on the ring structure of bacterial GroEL or other chaperone polypeptides. Other non-immunoglobulin based scaffolds which may be used include those based on the LDL receptor class A, EGF domain monomers and multimers, and scaffolds available from Biorexis (King of Prussia, PA) or Avidia (Mountain View, CA). Other non-immunoglobulin scaffolds which may be used are described, for example, in WO 05/040229, WO 04/044011, and US 2005/0089932.

3.1.2. Selection of the Main-Chain Conformation

The members of the immunoglobulin superfamily all share a similar fold for their polypeptide chain. For example, although antibodies are highly diverse in terms of their primary sequence, comparison of sequences and crystallographic structures has revealed that, contrary to expectation, five of the six antigen binding loops of antibodies (H1, H2, L1, L2, L3) adopt a limited number of main-chain conformations, or canonical structures (Chothia and Lesk (1987) *J. Mol. Biol.*, 196: 901; Chothia *et al.* (1989) *Nature*, 342: 877). Analysis of loop lengths and key residues has therefore enabled prediction of the main-chain conformations of H1, H2, L1, L2, and L3 found in the majority of human antibodies (Chothia *et al.* (1992) *J. Mol. Biol.*, 227: 799; Tomlinson *et al.* (1995) *EMBO J.*, 14: 4628; Williams *et al.* (1996) *J. Mol. Biol.*, 264: 220). Although the H3 region is much more diverse in terms of sequence, length, and structure (due to the use of D segments), it also forms a limited number of main-chain conformations for short loop

lengths which depend on the length and the presence of particular residues, or types of residues, at key positions in the loop and the antibody framework (Martin *et al.* (1996) *J. Mol. Biol.*, 263: 800; Shirai *et al.* (1996) *FEBS Letters*, 399: 1).

The ligands disclosed herein can be selected and/or assembled from libraries of domains, such as libraries of V_H domains and/or libraries of V_L domains. Moreover, the ligands disclosed herein may themselves be provided in the form of libraries. In one aspect disclosed herein, libraries of ligands and/or domains are designed in which certain loop lengths and key residues have been chosen to ensure that the main-chain conformation of the members is known. Advantageously, these are real conformations of immunoglobulin superfamily molecules found in nature, to minimize the chances that they are non-functional, as discussed above. Germline V gene segments serve as one exemplary basic framework for constructing antibody or T cell receptor libraries; other sequences are also of use. Variations may occur at a low frequency, such that a small number of functional members may possess an altered main-chain conformation, which does not affect its function.

Canonical structure theory is also of use to assess the number of different main-chain conformations encoded by ligands, to predict the main-chain conformation based on ligand sequences and to choose residues for diversification which do not affect the canonical structure. It is known that, in the human V_κ domain, the L1 loop can adopt one of four canonical structures, the L2 loop has a single canonical structure and that 90% of human V_κ domains adopt one of four or five canonical structures for the L3 loop (Tomlinson *et al.* (1995) *supra*); thus, in the V_κ domain alone, different canonical structures can combine to create a range of different main-chain conformations. Given that the V_λ domain encodes a different range of canonical structures for the L1, L2, and L3 loops, and that V_κ and V_λ domains can pair with any V_H domain which can encode several canonical structures for the H1 and H2 loops, the number of canonical structure combinations observed for these five loops is very large. This implies that the generation of diversity in the main-chain conformation may be essential for the production of a wide range of binding specificities. However, by constructing an antibody library based on a single known main-chain conformation it has been found, contrary to expectation, that diversity in the main-chain conformation is not required to generate sufficient diversity to target substantially all antigens. Even more surprisingly, the single main-chain conformation need not be a consensus structure. A single naturally occurring

conformation can be used as the basis for an entire library. Thus, in one aspect, the ligands disclosed herein possess a single known main-chain conformation.

The single main-chain conformation that is chosen is in an aspect, commonplace among molecules of the immunoglobulin superfamily type in question. A conformation is commonplace when a significant number of naturally occurring molecules are observed to adopt it. Accordingly, in one aspect disclosed herein, the natural occurrence of the different main-chain conformations for each binding loop of an immunoglobulin domain are considered separately and then a naturally occurring variable domain is chosen which possesses the desired combination of main-chain conformations for the different loops. If none is available, the nearest equivalent may be chosen. It is preferable that the desired combination of main-chain conformations for the different loops is created by selecting germline gene segments which encode the desired main-chain conformations. It is more preferable, that the selected germline gene segments are frequently expressed in nature, and most preferable that they are the most frequently expressed of all natural germline gene segments.

In designing ligands or libraries thereof the incidence of the different main-chain conformations for each of the antigen binding loops may be considered separately. For H1, H2, L1, L2, and L3, a given conformation that is adopted by between 20% and 100% of the antigen binding loops of naturally occurring molecules is chosen. Typically, its observed incidence is above 35% (i.e. between 35% and 100%) and, ideally, above 50% or even above 65%. Since the vast majority of H3 loops do not have canonical structures, it is preferable to select a main-chain conformation which is commonplace among those loops which do display canonical structures. For each of the loops, the conformation which is observed most often in the natural repertoire is therefore selected. In human antibodies, the most popular canonical structures (CS) for each loop are as follows: H1 - CS 1 (79% of the expressed repertoire), H2 - CS 3 (46%), L1 - CS 2 of V_κ (39%), L2 - CS 1 (100%), L3 - CS 1 of V_κ (36%) (calculation assumes a κ:λ ratio of 70:30, Hood *et al.* (1967) *Cold Spring Harbor Symp. Quant. Biol.*, 48: 133). For H3 loops that have canonical structures, a CDR3 length (Kabat *et al.* (1991) *Sequences of proteins of immunological interest*, U.S. Department of Health and Human Services) of seven residues with a salt-bridge from residue 94 to residue 101 appears to be the most common. There are at least 16 human antibody sequences in the EMBL data library with the required H3 length and key residues to form this conformation and at least two

crystallographic structures in the protein data bank which can be used as a basis for antibody modeling (2cgr and 1tet). The most frequently expressed germline gene segments that this combination of canonical structures are the V_H segment 3-23 (DP-47), the J_H segment JH4b, the V_κ segment O2/O12 (DPK9) and the J_κ segment $J_\kappa 1$. V_H segments DP45 and DP38 are also suitable. These segments can therefore be used in combination as a basis to construct a library with the desired single main-chain conformation.

Alternatively, instead of choosing the single main-chain conformation based on the natural occurrence of the different main-chain conformations for each of the binding loops in isolation, the natural occurrence of combinations of main-chain conformations is used as the basis for choosing the single main-chain conformation. In the case of antibodies, for example, the natural occurrence of canonical structure combinations for any two, three, four, five, or for all six of the antigen binding loops can be determined. Here, it is preferable that the chosen conformation is commonplace in naturally occurring antibodies and most preferable that it observed most frequently in the natural repertoire. Thus, in human antibodies, for example, when natural combinations of the five antigen binding loops, H1, H2, L1, L2, and L3, are considered, the most frequent combination of canonical structures is determined and then combined with the most popular conformation for the H3 loop, as a basis for choosing the single main-chain conformation.

3.2. Preparation of Domain Antibodies

Domain antibodies are prepared in a number of ways. For each of these approaches, well-known methods of preparing (e.g., amplifying, mutating, etc.) and manipulating nucleic acid sequences are applicable.

One means of preparing a domain antibody is to amplify and express the V_H or V_L region of a heavy chain or light chain gene for a cloned antibody known to bind the desired antigen. That is, the V_H or V_L domain of a known domain antibody coding region can be amplified and expressed as a single domain (or as a fusion of a single domain) and evaluated for binding to CD28. The boundaries of V_H and V_L domains are set out by Kabat et al. (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.). The information regarding the boundaries of the V_H and V_L domains of heavy and light chain genes is used to design

PCR primers that amplify the V domain from a cloned heavy or light chain coding sequence encoding an antibody known to bind CD28. The amplified V domain is inserted into a suitable expression vector, e.g., pHEN-1 (Hoogenboom et al. (1991) *Nucleic Acids Res.* 19: 4133-4137) and expressed, either alone or as a fusion with another polypeptide sequence.

The V_H gene is produced by the recombination of three gene segments, V_H, D and J_H. In humans, there are approximately 51 functional V_H segments (Cook and Tomlinson (1995) *Immunol Today* 16: 237), 25 functional D segments (Corbett et al. (1997) *J. Mol. Biol.* 268: 69) and 6 functional J_H segments (Ravetch et al. (1981) *Cell* 27: 583), depending on the haplotype. The V_H segment encodes the region of the polypeptide chain which forms the first and second antigen binding loops of the V_H domain (H1 and H2), while the V_H, D and J_H segments combine to form the third antigen binding loop of the V_H domain (H3).

The V_L gene is produced by the recombination of only two gene segments, V_L and J_L. In humans, there are approximately 40 functional V_κ segments (Schäble and Zachau (1993) *Biol. Chem. Hoppe-Seyler* 374: 1001), 31 functional V_λ segments (Williams et al. (1996) *J. Mol. Biol.* 264: 220; Kawasaki et al. (1997) *Genome Res.* 7: 250), 5 functional J_κ segments (Hieter et al. (1982) *J. Biol. Chem.* 257: 1516) and 4 functional J_λ segments (Vasicek and Leder (1990) *J. Exp. Med.* 172: 609), depending on the haplotype. The V_L segment encodes the region of the polypeptide chain which forms the first and second antigen binding loops of the V_L domain (L1 and L2), while the V_L and J_L segments combine to form the third antigen binding loop of the V_L domain (L3). Antibodies selected from this primary repertoire are believed to be sufficiently diverse to bind almost all antigens with at least moderate affinity. High affinity antibodies are produced *in vivo* by "affinity maturation" of the rearranged genes, in which point mutations are generated and selected by the immune system on the basis of improved binding.

In one approach, a repertoire of V_H or V_L domains, in an aspect, human V_H or V_L domains, is screened by, for example, phage display, panning against the desired antigen. Methods for the construction of bacteriophage display libraries and lambda phage expression libraries are well known in the art, and taught, for example, by: McCafferty et al. (1990) *Nature* 348: 552; Kang et al. (1991) *Proc. Natl. Acad. Sci. U.S.A.*, 88: 4363;

Clackson et al. (1991) *Nature* 352: 624; Lowman et al. (1991) *Biochemistry* 30: 10832; Burton et al. (1991) *Proc. Natl. Acad. Sci U.S.A.* 88: 10134; Hoogenboom et al. (1991) *Nucleic Acids Res.* 19: 4133; Chang et al. (1991) *J. Immunol.* 147: 3610; Breitling et al. (1991) *Gene* 104: 147; Marks et al. (1991) *J. Mol. Biol.* 222: 581; Barbas et al. (1992) *Proc. Natl. Acad. Sci. U.S.A.* 89: 4457; Hawkins and Winter (1992) *J. Immunol.*, 22: 867; Marks et al. (1992) *J. Biol. Chem.*, 267: 16007; and Lerner et al. (1992) *Science*, 258: 1313. Fab phage display libraries are taught, for example, by U.S. 5,922,545. scFv phage libraries are taught, for example, by Huston et al. (1988) *Proc. Natl. Acad. Sci U.S.A.* 85: 5879-5883; Chaudhary et al. (1990) *Proc. Natl. Acad. Sci U.S.A.* 87: 1066-1070; McCafferty et al. (1990) *supra*; Clackson et al. (1991) *supra*; Marks et al. (1991) *supra*; Chiswell et al. (1992) *Trends Biotech.* 10: 80; and Marks et al. (1992) *supra*. Various embodiments of scFv libraries displayed on bacteriophage coat proteins have been described. Refinements of phage display approaches are also known, for example as described in WO96/06213 and WO92/01047 (Medical Research Council et al.) and WO97/08320 (Morphosys, *supra*).

The repertoire of V_H or V_L domains can be a naturally-occurring repertoire of immunoglobulin sequences or a synthetic repertoire. A naturally-occurring repertoire is one prepared, for example, from immunoglobulin-expressing cells harvested from one or more individuals. Such repertoires can be "naïve," i.e., prepared, for example, from human fetal or newborn immunoglobulin-expressing cells, or rearranged, i.e., prepared from, for example, adult human B cells. Natural repertoires are described, for example, by Marks et al. (1991) *J. Mol. Biol.* 222: 581 and Vaughan et al. (1996) *Nature Biotech.* 14: 309. If desired, clones identified from a natural repertoire, or any repertoire, for that matter, that bind the target antigen are then subjected to mutagenesis and further screening in order to produce and select variants with improved binding characteristics.

Synthetic repertoires of domain antibodies are prepared by artificially introducing diversity into a cloned V domain. Synthetic repertoires are described, for example, by Hoogenboom & Winter (1992) *J. Mol. Biol.* 227: 381; Barbas et al. (1992) *Proc. Natl. Acad. Sci. U.S.A.* 89: 4457; Nissim et al. (1994) *EMBO J.* 13: 692; Griffiths et al. (1994) *EMBO J.* 13: 3245; DeKriuf et al. (1995) *J. Mol. Biol.* 248: 97; and WO 99/20749.

In one aspect, synthetic variable domain repertoires are prepared in V_H or $V\kappa$ backgrounds, based on artificially diversified germline V_H or $V\kappa$ sequences. For example, the V_H domain repertoire can be based on cloned germline V_H gene segments

V3-23/DP47 (Tomlinson et al. (1992) *J. Mol. Biol.* 227: 776) and JH4b. The V_κ domain repertoire can be based, for example, on germline V_κ gene segments O2/O12/DPK9 (Cox et al. (1994) *Eur. J. Immunol.* 24: 827) and $J_\kappa 1$. Diversity is introduced into these or other gene segments by, for example, PCR mutagenesis. Diversity can be randomly introduced, for example, by error prone PCR (Hawkins, et al. (1992) *J. Mol. Biol.* 226: 889) or chemical mutagenesis. As discussed above, however, in one embodiment the introduction of diversity is targeted to particular residues. In another embodiment the desired residues are targeted by introduction of the codon NNK using mutagenic primers (using the IUPAC nomenclature, where N = G, A, T or C, and K = G or T), which encodes all amino acids and the TAG stop codon. Other codons which achieve similar ends are also of use, including the NNN codon (which leads to the production of the additional stop codons TGA and TAA), DVT codon ((A/G/T) (A/G/C)T), DVC codon ((A/G/T)(A/G/C)C), and DVY codon ((A/G/T)(A/G/C)(C/T). The DVT codon encodes 22% serine and 11% tyrosine, asparagine, glycine, alanine, aspartate, threonine and cysteine, which most closely mimics the distribution of amino acid residues for the antigen binding sites of natural human antibodies. Repertoires are made using PCR primers having the selected degenerate codon or codons at each site to be diversified. PCR mutagenesis is well known in the art.

In one aspect, diversity is introduced into the sequence of human germline V_H gene segments V3-23/DP47 (Tomlinson et al. (1992) *J. Mol. Biol.* 227: 7768) and JH4b using the NNK codon at sites H30, H31, H33, H35, H50, H52, H52a, H53, H55, H56, H58, H95, H97, and H98, corresponding to diversity in CDRs 1, 2 and 3, with the numbering as used in U.S. Patent No. 6,696,245.

In another aspect, diversity is also introduced into the sequence of human germline V_H gene segments V3-23/DP47 and JH4b, for example, using the NNK codon at sites H30, H31, H33, H35, H50, H52, H52a, H53, H55, H56, H58, H95, H97, H98, H99, H100, H100a, and H100b, corresponding to diversity in CDRs 1, 2 and 3, with the numbering as used in U.S. Patent No. 6,696,245.

In another aspect, diversity is introduced into the sequence of human germline V_κ gene segments O2/O12/DPK9 and $J_\kappa 1$, for example, using the NNK codon at sites L30, L31, L32, L34, L50, L53, L91, L92, L93, L94, and L96, corresponding to diversity in CDRs 1, 2 and 3,with the numbering as used in U.S. Patent No. 6,696,245.

Diversified repertoires are cloned into phage display vectors as known in the art and as described, for example, in WO 99/20749. In general, the nucleic acid molecules and vector constructs required for the compositions and methods set forth herein are available in the art and are constructed and manipulated as set forth in standard laboratory manuals, such as Sambrook et al. (1989), Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, USA and subsequent editions.

The manipulation of nucleic acids as set forth herein is typically carried out in recombinant vectors. As used herein, "vector" refers to a discrete element that is used to introduce heterologous DNA into cells for the expression and/or replication thereof. Methods by which to select or construct and, subsequently, use such vectors are well known to one of skill in the art. Numerous vectors are publicly available, including bacterial plasmids, bacteriophage, artificial chromosomes and episomal vectors. Such vectors may be used for simple cloning and mutagenesis; alternatively, as is typical of vectors in which repertoire (or pre-repertoire) members herein are carried, a gene expression vector is employed. A vector of use set forth herein is selected to accommodate a polypeptide coding sequence of a desired size, typically from 0.25 kilobase (kb) to 40 kb in length. A suitable host cell is transformed with the vector after *in vitro* cloning manipulations. Each vector contains various functional components, which generally include a cloning (or "polylinker") site, an origin of replication and at least one selectable marker gene. If a given vector is an expression vector, it additionally possesses one or more of the following: enhancer element, promoter, transcription termination and signal sequences, each positioned in the vicinity of the cloning site, such that they are operatively linked to the gene encoding a polypeptide repertoire member as set forth herein.

Both cloning and expression vectors generally contain nucleic acid sequences that enable the vector to replicate in one or more selected host cells. Typically in cloning vectors, this sequence is one that enables the vector to replicate independently of the host chromosomal DNA and includes origins of replication or autonomously replicating sequences. Such sequences are well known for a variety of bacteria, yeast and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 micron plasmid origin is suitable for yeast, and various viral origins (e.g. SV 40, adenovirus) are useful for cloning vectors in mammalian cells. Generally, the

origin of replication is not needed for mammalian expression vectors unless these are used in mammalian cells able to replicate high levels of DNA, such as COS cells.

Advantageously, a cloning or expression vector also contains a selection gene also referred to as selectable marker. This gene encodes a protein necessary for the survival or growth of transformed host cells grown in a selective culture medium. Host cells not transformed with the vector containing the selection gene will therefore not survive in the culture medium. Typical selection genes encode proteins that confer resistance to antibiotics and other toxins, e.g. ampicillin, neomycin, methotrexate or tetracycline, complement auxotrophic deficiencies, or supply critical nutrients not available in the growth media.

Because the replication of vectors herein is most conveniently performed in *E. coli*, an *E. coli*-selectable marker, for example, the β-lactamase gene that confers resistance to the antibiotic ampicillin, is of use. These can be obtained from *E. coli* plasmids, such as pBR322 or a pUC plasmid such as pUC18 or pUC19. However, other plasmid microorganism combinations can also be reasonably substituted.

Expression vectors usually contain a promoter that is recognized by the host organism and is operably linked to the coding sequence of interest. Such a promoter may be inducible or constitutive. The term "operably linked" refers to a juxtaposition wherein the components described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences.

Promoters suitable for use with prokaryotic hosts include, for example, the β-lactamase and lactose promoter systems, alkaline phosphatase, the tryptophan (trp) promoter system and hybrid promoters such as the tac promoter. Promoters for use in bacterial systems will also generally contain a Shine-Dalgarno sequence operably linked to the coding sequence.

In libraries or repertoires as described herein, vectors may be expression vectors that enable the expression of a nucleotide sequence corresponding to a polypeptide library member. Thus, selection is performed by separate propagation and expression of a single clone expressing the polypeptide library member or by use of any selection display system. As described above, one selection display system uses bacteriophage

display. Thus, phage or phagemid vectors can be used. Vectors may be phagemid vectors, which have an E. coli origin of replication (for double stranded replication) and also a phage origin of replication (for production of single-stranded DNA). The manipulation and expression of such vectors is well known in the art (Hoogenboom and Winter (1992) *supra*; Nissim et al. (1994) *supra*). Briefly, the vector contains a β-lactamase or other selectable marker gene to confer selectivity on the phagemid, and a lac promoter upstream of a expression cassette that consists (N to C terminal) of a pelB leader sequence (which directs the expressed polypeptide to the periplasmic space), a multiple cloning site (for cloning the nucleotide version of the library member), optionally, one or more peptide tags (for detection), optionally, one or more TAG stop codons and the phage protein pIII. In one embodiment, the vector encodes, rather than the pelB leader sequence, a eukaryotic GAS1 leader sequence which serves to direct the secretion of the fusion polypeptide to the periplasmic space in E. coli or to the medium in eukaryotic cell systems. Using various suppressor and non-suppressor strains of E. coli and with the addition of glucose, iso-propyl thio-β-D-galactoside (IPTG) or a helper phage, such as VCS M13, the vector is able to replicate as a plasmid with no expression, produce large quantities of the polypeptide library member only, or produce phage, some of which contain at least one copy of the polypeptide-pIII fusion on their surface.

An example of a vector is the pHEN1 phagemid vector (Hoogenboom et al. (1991) *Nucl. Acids Res.* 19: 4133-4137; sequence is available, e.g., as SEQ ID NO:7 in WO 03/031611), in which the production of pIII fusion protein is under the control of the LacZ promoter, which is inhibited in the presence of glucose and induced with IPTG. When grown in suppressor strains of E. coli, e.g., TG1, the gene III fusion protein is produced and packaged into phage, while growth in non-suppressor strains, e.g., HB2151, permits the secretion of soluble fusion protein into the bacterial periplasm and into the culture medium. Because the expression of gene III prevents later infection with helper phage, the bacteria harboring the phagemid vectors are propagated in the presence of glucose before infection with VCSM13 helper phage for phage rescue.

Construction of vectors as set forth herein employs conventional ligation techniques. Isolated vectors or DNA fragments are cleaved, tailored, and re-ligated in the form desired to generate the required vector. If desired, sequence analysis to confirm that the correct sequences are present in the constructed vector is performed using standard methods. Suitable methods for constructing expression vectors, preparing *in vitro*

transcripts, introducing DNA into host cells, and performing analyses for assessing expression and function are known to those skilled in the art. The presence of a gene sequence in a sample is detected, or its amplification and/or expression quantified by conventional methods, such as Southern or Northern analysis, Western blotting, dot blotting of DNA, RNA or protein, in situ hybridization, immunocytochemistry or sequence analysis of nucleic acid or protein molecules. Those skilled in the art will readily envisage how these methods may be modified, if desired.

3.3. Screening Domain Antibodies for Antigen Binding

Following expression of a repertoire of domain antibodies on the surface of phage, selection is performed by contacting the phage repertoire with immobilized target antigen, washing to remove unbound phage, and propagation of the bound phage, the whole process frequently referred to as "panning". This process is applicable to the screening of domain antibodies as well as other antibody fragments that can be expressed on a display library, e.g., scFv, Fab, etc. Alternatively, phage are pre-selected for the expression of properly folded member variants by panning against an immobilized generic ligand (e.g., protein A or protein L) that is only bound by folded members. This has the advantage of reducing the proportion of non-functional members, thereby increasing the proportion of members likely to bind a target antigen. Pre-selection with generic ligands is taught in WO 99/20749, for example. The screening of phage antibody libraries is generally described, for example, by Harrison et al. (1996) *Meth. Enzymol.* 267: 83-109.

Screening is commonly performed using purified antigen immobilized on a solid support, for example, plastic tubes or wells, or on a chromatography matrix, for example Sepharose™ (Pharmacia). Screening or selection can also be performed on complex antigens, such as the surface of cells (Marks et al. (1993) *BioTechnology* 11: 1145; de Kruif et al. (1995) *Proc. Natl. Acad. Sci.* U.S.A. 92: 3938). Another alternative involves selection by binding biotinylated antigen in solution, followed by capture on streptavidin-coated beads.

In one aspect, panning is performed by immobilizing antigen (generic or specific) on tubes or wells in a plate, e.g., Nunc MAXISORP™ immunotube 8 well strips. Wells are coated with 150 µl of antigen (100 µg/ml in PBS) and incubated overnight. The wells are then washed 3 times with PBS and blocked with 400 µl PBS-2% skim milk (2%

MPBS) at 37°C for 2 hr. The wells are rinsed 3 times with PBS and phage are added in 2%MPBS. The mixture is incubated at room temperature for 90 minutes and the liquid, containing unbound phage, is removed. Wells are rinsed 10 times with PBS-0.1% Tween 20, and then 10 times with PBS to remove detergent. Bound phage are eluted by adding 200 µl of freshly prepared 100 mM triethylamine, mixing well and incubating for 10 min at room temperature. Eluted phage are transferred to a tube containing 100 µl of 1 M Tris-HCl, pH 7.4 and vortexed to neutralize the triethylamine. Exponentially-growing E. coli host cells (e.g., TG1) are infected with, for example, 150 ml of the eluted phage by incubating for 30 min at 37°C. Infected cells are spun down, resuspended in fresh medium and plated in top agarose. Phage plaques are eluted or picked into fresh cultures of host cells to propagate for analysis or for further rounds of selection. One or more rounds of plaque purification are performed if necessary to ensure pure populations of selected phage. Other screening approaches are described by Harrison et al. (1996) *supra*.

Following identification of phage expressing a domain antibody that binds a desired target, if a phagemid vector such as pHEN1 has been used, the variable domain fusion proteins are easily produced in soluble form by infecting non-suppressor strains of bacteria, e.g., HB2151 that permit the secretion of soluble gene III fusion protein. If a GAS1 secretion signal peptide is encoded by the vector, the fusion polypeptide can be secreted by eukaryotic (e.g., yeast or mammalian) or prokaryotic (e.g., *E. coli*) cells. Alternatively, the V domain sequence can be sub-cloned into an appropriate expression vector to produce soluble protein according to methods known in the art.

3.4. Purification and Concentration of Domain Antibodies

Domain antibodies secreted into the periplasmic space or into the medium of bacteria are harvested and purified according to known methods (Harrison et al. (1996) *supra*). Skerra & Pluckthun (1988) *Science* 240: 1038 and Breitling et al. (1991) *Gene* 104: 147 describe the harvest of domain antibodies from the periplasm, and Better et al. (1988) *Science* 240: 1041 describes harvest from the culture supernatant. For some domain antibodies, purification can also be achieved by binding to generic ligands, such as protein A or Protein L. Alternatively, the variable domains can be expressed with a peptide tag, e.g., the Myc, HA or 6X-His tags (SEQ ID NO: 644), which facilitate purification by affinity chromatography.

If necessary, domain antibodies are concentrated by any of several methods well known in the art, including, for example, ultrafiltration, diafiltration and tangential flow filtration. The process of ultrafiltration uses semi-permeable membranes and pressure to separate molecular species on the basis of size and shape. The pressure is provided by gas pressure or by centrifugation. Commercial ultrafiltration products are widely available, e.g., from Millipore (Bedford, MA; examples include the Centricon™ and Microcon™ concentrators) and Vivascience (Hannover, Germany; examples include the Vivaspin™ concentrators). By selection of a molecular weight cutoff smaller than the target polypeptide (usually 1/3 to 1/6 the molecular weight of the target polypeptide, although differences of as little as 10 kD can be used successfully), the polypeptide is retained when solvent and smaller solutes pass through the membrane. Thus, a molecular weight cutoff of about 5 kD is useful for concentration of domain antibodies described herein.

Diafiltration, which uses ultrafiltration membranes with a "washing" process, is used where it is desired to remove or exchange the salt or buffer in a polypeptide preparation. The polypeptide is concentrated by the passage of solvent and small solutes through the membrane, and remaining salts or buffer are removed by dilution of the retained polypeptide with a new buffer or salt solution or water, as desired, accompanied by continued ultrafiltration. In continuous diafiltration, new buffer is added at the same rate that filtrate passes through the membrane. A diafiltration volume is the volume of polypeptide solution prior to the start of diafiltration – using continuous diafiltration, greater than 99.5% of a fully permeable solute can be removed by washing through six diafiltration volumes with the new buffer. Alternatively, the process can be performed in a discontinuous manner, wherein the sample is repeatedly diluted and then filtered back to its original volume to remove or exchange salt or buffer and ultimately concentrate the polypeptide. Equipment for diafiltration and detailed methodologies for its use are available, for example, from Pall Life Sciences (Ann Arbor, MI) and Sartorius AG/Vivascience (Hannover, Germany).

Tangential flow filtration (TFF), also known as "cross-flow filtration," also uses ultrafiltration membrane. Fluid containing the target polypeptide is pumped tangentially along the surface of the membrane. The pressure causes a portion of the fluid to pass through the membrane while the target polypeptide is retained above the filter. In contrast to standard ultrafiltration, however, the retained molecules do not accumulate on

the surface of the membrane, but are carried along by the tangential flow. The solution that does not pass through the filter (containing the target polypeptide) can be repeatedly circulated across the membrane to achieve the desired degree of concentration. Equipment for TFF and detailed methodologies for its use are available, for example, from Millipore (e.g., the ProFlux M12™ Benchtop TFF system and the Pellicon™ systems), Pall Life Sciences (e.g., the Minim™ Tangential Flow Filtration system).

Protein concentration is measured in a number of ways that are well known in the art. These include, for example, amino acid analysis, absorbance at 280 nm, the "Bradford" and "Lowry" methods, and SDS-PAGE. The most accurate method is total hydrolysis followed by amino acid analysis by HPLC, concentration is then determined then comparison with the known sequence of the domain antibody. While this method is the most accurate, it is expensive and time-consuming. Protein determination by measurement of UV absorbance at 280 nm faster and much less expensive, yet relatively accurate and is a compromise over amino acid analysis. Absorbance at 280 nm was used to determine protein concentrations reported in the Examples described herein.

"Bradford" and "Lowry" protein assays (Bradford (1976) *Anal. Biochem.* 72: 248-254; Lowry et al. (1951) *J. Biol. Chem.* 193: 265-275) compare sample protein concentration to a standard curve most often based on bovine serum albumin (BSA). These methods are less accurate, tending to underestimate the concentration of domain antibodies. Their accuracy could be improved, however, by using a V_H or V_κ single domain polypeptide as a standard.

An additional protein assay method that can be utilized is the bicinchoninic acid assay described in U.S. Patent No. 4,839,295 (incorporated herein by reference) and marketed by Pierce Biotechnology (Rockford, IL) as the "BCA Protein Assay" (e.g., Pierce Catalog No. 23227).

The SDS-PAGE method uses gel electrophoresis and Coomassie Blue staining in comparison to known concentration standards, e.g., known amounts of a domain antibody. Quantitation can be done by eye or by densitometry.

Domain antibodies described herein retain solubility at high concentration (e.g., at least 4.8 mg (~400 μM) in aqueous solution (e.g., PBS), and in an aspect, at least about 5 mg/ml (~417 μM), 10 mg/ml (~833 μM), 20 mg/ml (~1.7 mM), 25 mg/ml (~2.1 mM), 30 mg/ml (~2.5 mM), 35 mg/ml (~2.9 mM), 40 mg/ml (~3.3 mM), 45 mg/ml (~3.75 mM),

50 mg/ml (~4.2 mM), 55 mg/ml (~4.6 mM), 60 mg/ml (~5.0 mM), 65 mg/ml (~5.4 mM), 70 mg/ml (~5.8 mM), 75 mg/ml (~6.3 mM), 100 mg/ml (~8.33 mM), 150 mg/ml (~12.5 mM), 200 mg/ml (~16.7 mM), 240 mg/ml (~20 mM) or higher). One structural feature that promotes high solubility is the relatively small size of the domain antibodies. A full length conventional four chain antibody, e.g., IgG is about 150 kD in size. In contrast, domain antibodies, which have a general structure comprising 4 framework (FW) regions and 3 CDRs, have a size of approximately 12 kD, or less than 1/10 the size of a conventional antibody. Similarly, domain antibodies are approximately half the size of a scFv molecule (~26 kD), and approximately one-fifth the size of a Fab molecule (~60 kD). The size of a domain antibody-containing structure disclosed herein may be 100 kD or less, including structures of, for example, about 90 kD or less, 80 kD or less, 70 kD or less, 60 kD or less, 50 kD or less, 40 kD or less, 30 kD or less, 20 kD or less, down to and including about 12 kD, or a domain antibody in isolation.

The solubility of a domain antibody is primarily determined by the interactions of the amino acid side chains with the surrounding solvent. Hydrophobic side chains tend to be localized internally as a polypeptide folds, away from the solvent-interacting surfaces of the polypeptide. Conversely, hydrophilic residues tend to be localized at the solvent-interacting surfaces of a polypeptide. Generally, polypeptides having a primary sequence that permits the molecule to fold to expose more hydrophilic residues to the aqueous environment are more soluble than one that folds to expose fewer hydrophilic residues to the surface. Thus, the arrangement and number of hydrophobic and hydrophilic residues is an important determinant of solubility. Other parameters that determine polypeptide solubility include solvent pH, temperature, and ionic strength. In a common practice, the solubility of polypeptides can be maintained or enhanced by the addition of glycerol (e.g., ~10% v/v) to the solution.

As discussed above, specific amino acid residues have been identified in conserved residues of human V_H domains that vary in the V_H domains of camelid species, which are generally more soluble than human V_H domains. These include, for example, Gly 44 (Glu in camelids), Leu 45 (Arg in camelids) and Trp 47 (Gly in camelids). Amino acid residue 103 of V_H is also implicated in solubility, with mutation from Trp to Arg tending to confer increased V_H solubility.

In some aspects as set forth herein, domain antibodies are based on the DP47 germline V_H gene segment or the DPK9 germline V_κ gene segment. Thus, these germline

gene segments are capable, particularly when diversified at selected structural locations described herein, of producing specific binding domain antibodies that are highly soluble. In particular, the four framework regions, which are, in an aspect, not diversified, can contribute to the high solubility of the resulting proteins.

It is expected that a domain antibody that shares a percent sequence identity with one having a known high solubility will also tend to be highly soluble. Thus, as one means of prediction or recognition that a given domain antibody would have the high solubility recited herein, one can compare the sequence of a domain antibody to one or more domain antibodies having known solubility. Thus, when a domain antibody is identified that has high binding affinity but unknown solubility, comparison of its amino acid sequence with that of one or more (in an aspect, more) domain antibodies known to have high solubility (e.g., a dAb sequence disclosed herein) can permit prediction of its solubility. While it is not an absolute predictor, where there is a high degree of similarity to a known highly soluble sequence, e.g., 90-95% or greater similarity, and particularly where there is a high degree of similarity with respect to hydrophilic amino acid residues, or residues likely to be exposed at the solvent interface, it is more likely that a newly identified binding polypeptide will have solubility similar to that of the known highly soluble sequence.

Molecular modeling software can also be used to predict the solubility of a polypeptide sequence relative to that of a polypeptide of known solubility. For example, the substitution or addition of a hydrophobic residue at the solvent-exposed surface, relative to a molecule of known solubility that has a less hydrophobic or even hydrophilic residue exposed in that position is expected to decrease the relative solubility of the polypeptide. Similarly, the substitution or addition of a more hydrophilic residue at such a location is expected to increase the relative solubility. That is, a change in the net number of hydrophilic or hydrophobic residues located at the surface of the molecule (or the overall hydrophobic or hydrophilic nature of the surface-exposed residues) relative to a domain antibody structure with known solubility can predict the relative solubility of a domain antibody.

Alternatively, or in conjunction with such prediction, one can determine limits of a domain antibody's solubility by simply concentrating the polypeptide.

3.5. Affinity Determination

Isolated domain antibody-containing polypeptides as described herein, in an aspect, have affinities (dissociation constant, $K_d = K_{off}/K_{on}$) of at least about 500 nM or less, and in an aspect, at least about 400 nM-50 pM, 300 nM-50 pM, 200 nM – 50 pM, and in a further aspect, at least 100 nM – 50 pM, 75 nM – 50 pM, 50 nM – 50 pM, 25 nM – 50 pM, 10 nM – 50 pM, 5 nM – 50 pM, 1 nM – 50 pM, 950 pM – 50 pM, 900 pM – 50 pM, 850 pM – 50 pM, 800 pM – 50 pM, 750 pM – 50 pM, 700 pM – 50 pM, 650 pM – 50 pM, 600 pM – 50 pM, 550 pM – 50 pM, 500 pM – 50 pM, 450 pM – 50 pM, 400 pM – 50 pM, 350 pM – 50 pM, 300 pM – 50 pM, 250 pM – 50 pM, 200 pM – 50 pM, 150 pM – 50 pM, 100 pM – 50 pM, 90 pM – 50 pM, 80 pM – 50 pM, 70 pM – 50 pM, 60 pM – 50 pM, or even as low as 50 pM.

In another embodiment, the domain antibody inhibits binding of CD28 to CD80 with an IC_{50} in the range of 1 pM to 1.5 μM, inclusive; IC_{50} for inhibition of CD28 binding to CD80. The IC_{50} can be in the range of 1 pM to 1 μM, 1 pM to 900 nM, 1 pM to 800 nM, 1 pM to 700 nM, 1 pM to 600 nM, 1 pM to 500 nM, 1 pM to 400 nM, 1 pM to 300 nM, 1 pM to 200 nM, 1 pM to 100 nM, 1 pM to 50 nM, 1 pM to 10 nM, 1 pM to 1 nM, 1 pM to 500 pM, 1 pM to 100 pM, 1 pM to 50 pM, 1 pM to 10 pM, or 1 pM to 5 pM. Further acceptable ranges include, for example, 50 pM to 1 μM, 100 pM to 500 nM, 125 pM to 250 nM, 150 pM to 200 nM, 150 pM to 100 nM, and 200 pM to 50 nM.

In another embodiment, the domain antibody inhibits binding of CD28 to CD86 with an IC_{50} in the range of 1 pM to 1.5 μM, inclusive; IC_{50} for inhibition of CD28 binding to CD86. The IC_{50} can be in the range of 1 pM to 1 μM, 1 pM to 900 nM, 1 pM to 800 nM, 1 pM to 700 nM, 1 pM to 600 nM, 1 pM to 500 nM, 1 pM to 400 nM, 1 pM to 300 nM, 1 pM to 200 nM, 1 pM to 100 nM, 1 pM to 50 nM, 1 pM to 10 nM, 1 pM to 1 nM, 1 pM to 500 pM, 1 pM to 100 pM, 1 pM to 50 pM, 1 pM to 10 pM, or 1 pM to 5 pM. Further acceptable ranges include, for example, 50 pM to 1 μM, 100 pM to 500 nM, 125 pM to 250 nM, 150 pM to 200 nM, 150 pM to 100 nM, and 200 pM to 50 nM.

The antigen-binding affinity of a domain antibody can be conveniently measured by Surface Plasmon Resonance (SPR) using the BIAcore system (Pharmacia Biosensor, Piscataway, N.J.). In this method, antigen is coupled to the BIAcore chip at known concentrations, and variable domain polypeptides are introduced. Specific binding between the variable domain polypeptide and the immobilized antigen results in

increased protein concentration on the chip matrix and a change in the SPR signal. Changes in SPR signal are recorded as resonance units (RU) and displayed with respect to time along the Y axis of a sensorgram. Baseline signal is taken with solvent alone (e.g., PBS) passing over the chip. The net difference between baseline signal and signal after completion of domain antibody injection represents the binding value of a given sample. To determine the off rate (K_{off}), on rate (K_{on}) and dissociation rate (K_d) constants, BIAcore kinetic evaluation software (e.g., version 2.1) is used.

Thus, SPR can be used to monitor antagonism of CD28 binding to CD80 or CD86 by a domain antibody preparation by measuring the displacement or inhibition of binding of CD28 to CD80 or CD86 caused the monovalent antibody preparation. SPR can also be used to monitor the dimerization, or in an aspect, the lack of dimerization, occurring via Fc region in antibody preparations as described herein.

High affinity is dependent upon the complementarity between a surface of the antigen and the CDRs of the antibody or antibody fragment. Complementarity is determined by the type and strength of the molecular interactions possible between portions of the target and the CDR, for example, the potential ionic interactions, van der Waals attractions, hydrogen bonding or other interactions that can occur. CDR3 tends to contribute more to antigen binding interactions than CDRs 1 and 2, probably due to its generally larger size, which provides more opportunity for favorable surface interactions. (*See, e.g.*, Padlan et al. (1994) *Mol. Immunol.* 31: 169-217; Chothia & Lesk (1987) *J. Mol. Biol.* 196: 904-917; and Chothia et al. (1985) *J. Mol. Biol.* 186: 651-663.) High affinity indicates domain antibody/antigen pairings that have a high degree of complementarity, which is directly related to the structures of the variable domain and the target.

In one aspect, a domain antibody is linked to another domain antibody to form a heterodimer in which each individual domain antibody is capable of binding a different cognate antigen. Fusing domain antibodies as heterodimers, wherein each monomer binds a different target antigen, can produce a dual-specific ligand capable, for example, of bridging the respective target antigens. Such dual specific ligands may be used to target cytokines and other molecules which cooperate synergistically in therapeutic situations in the body of an organism. Thus, there is provided a method for synergizing the activity of two or more cytokines, comprising administering a dual specific antibody heterodimer capable of binding to the two or more cytokines.

Domain antibodies set forth herein include CD28-binding domain antibody clones, and clones with substantial sequence similarity or percent identity to them that also bind target antigen with high affinity. As used herein, "substantial" sequence similarity or identity is at least 70% similarity or identity.

An additional measure of identity or similarity is the ability to hybridize under highly stringent hybridization conditions. Thus, a first sequence encoding a domain antibody is substantially similar to a second coding sequence if the first sequence hybridizes to the second sequence (or its complement) under highly stringent hybridization conditions (such as those described by Sambrook et al., Molecular Cloning, Laboratory Manuel, Cold Spring, Harbor Laboratory press, New York). "Highly stringent hybridization conditions" refer to hybridization in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C. "Very highly stringent hybridization conditions" refer to hybridization in 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C.

In an embodiment, domain antibodies include:

1h-239-850 (SEQ ID NO:58)
1h-35 (SEQ ID NO:59)
1h-36 (SEQ ID NO:60)
1h-79 (SEQ ID NO:61)
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1h-99-23737 (SEQ ID NO:635)

In an embodiment, domain antibodies may include one or more of the following CDRs:

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1h-80 CDR1 (SEQ ID NO:496)
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1h-108 CDR1 (SEQ ID NO:502)
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1h-108 CDR3 (SEQ ID NO:504)
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1h-203 CDR3 (SEQ ID NO:507)
1h-207 CDR1 (SEQ ID NO:508)
1h-207 CDR2 (SEQ ID NO:509)
1h-207 CDR3 (SEQ ID NO:510)
1h-238 CDR1 (SEQ ID NO:511)
1h-238 CDR2 (SEQ ID NO:512)
1h-238 CDR3 (SEQ ID NO:513)
1h-239 CDR1 (SEQ ID NO:514)
1h-239 CDR2 (SEQ ID NO:515)

1h-239 CDR3 (SEQ ID NO:516)
1h-99-237 CDR1 (SEQ ID NO:517)
1h-99-237 CDR2 (SEQ ID NO:518)
1h-99-237 CDR3 (SEQ ID NO:519)
1h-99-238 CDR1 (SEQ ID NO:520)
1h-99-238 CDR2 (SEQ ID NO:521)
1h-99-238 CDR3 (SEQ ID NO:522)
1h-37 CDR1 (SEQ ID NO:523)
1h-37 CDR2 (SEQ ID NO:524)
1h-37 CDR3 (SEQ ID NO:525)
1h-93 CDR1 (SEQ ID NO:526)
1h-93 CDR2 (SEQ ID NO:527)
1h-93 CDR3 (SEQ ID NO:528)
1h-99 CDR1 (SEQ ID NO:529)
1h-99 CDR2 (SEQ ID NO:530),
1h-99 CDR3 (SEQ ID NO:531),
1h-239-891 CDR1 (SEQ ID NO:636),
1h-239-891 CDR2 (SEQ ID NO:637), and
1h-239-891 CDR3 (SEQ ID NO:638).

4. Assays for CD28 Activities

In an exemplary embodiment, a domain antibody as described herein binds to CD28 yet does not substantially agonize CD28 signaling. Activation of the CD28 pathway manifests a number of different outcomes that can be measured in order to assess the effect of a given domain antibody on the activity of the pathway. However, for the assessment of the antagonist or agonist function of domain antibodies described herein, at least one of the following CD28 assays can be used.

In an embodiment, activation of T cells is measured. In the assay, human CD3 positive T cells are stimulated with anti-CD3 plus transfected CHO cells expressing either CD80 or CD86. This results in proliferation of the T cells and is CD28 dependent as domain antibodies block the proliferation response.

In another embodiment, induction of T cell proliferation and induction of cytokine secretion is measured. The assay comprises stimulation of human CD3 positive T cells

with anti-CD28 mAb 9.3 (Gibson, et al. (1996) *J. Biol. Chem.*, 271: 7079-7083). This results in up-regulation of T cell receptor-mediated signaling and secretion of cytokines and is CD28-dependent, as mAb 9.3 blocks the proliferation response. Secreted cytokines that may be measured include, but are not limited to, GM-CSF, IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-12 IL-13, IL-15, IL-17, IL-21, IL-22, IL-24, TGFβ, TNF-α, TNF-β, IFN-α, IFN-β, IFN-γ. One or more of such cytokines may be detected and/or measured according to the disclosure set forth herein.

As set forth elsewhere herein, an assay for CD28 activity may also include the assessment of CTLA4 activity. In particular, a domain antibody according to the present disclosure does not inhibit the CTLA-4-mediated inhibition of T cell function, including inhibition of T cell receptor mediated signaling, inhibition of T cell proliferation, and inhibition of cytokine secretion.

It will be understood, based on the disclosure herein, that domain antibodies set forth herein can possess multiple functions and activities, and therefore, may be assayed by multiple distinct assays. As set forth in detail elsewhere herein, domain antibodies have multiple defining characteristics (e.g., CD28 binding affinity, CDR domain identity, and amino acid sequence, among others), and therefore, each distinct domain antibody can be characterized in multiple ways and through multiple parameters. The characterization of each such domain antibody, alone or in conjunction with the activity and/or CD28 binding properties of the domain antibody, can therefore provide unique identifying characteristics for the domain antibody.

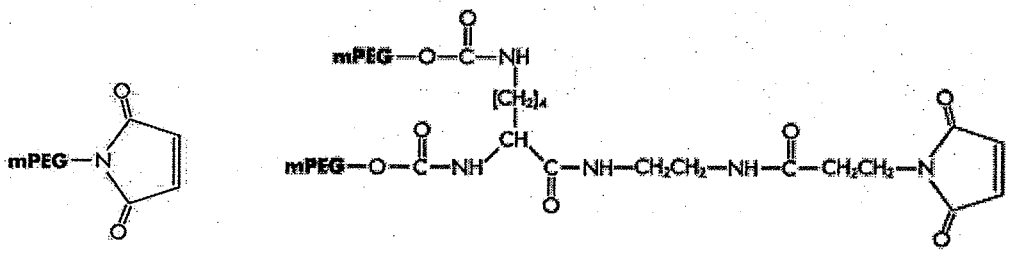
5. PEGylation of Domain Antibodies

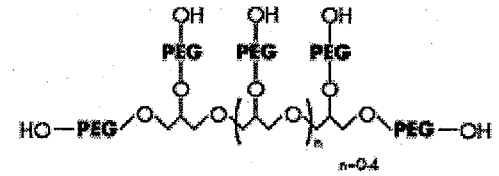
Also provided herein are PEGylated domain antibodies which have increased half-life and in an aspect, also resistance to degradation without a loss in activity (e.g., binding affinity) relative to non-PEGylated domain antibodies.

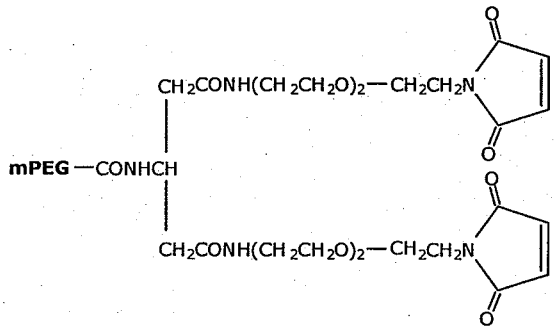
Both site-specific and random PEGylation of protein molecules is known in the art (See, for example, Zalipsky and Lee, *Poly(ethylene glycol) Chemistry: Biotechnical and Biomedical Applications* (1992) pp 347-370, Plenum, NY; Goodson and Katre (1990) *Bio/Technology,* 8: 343; Hershfield et al. (1991) *PNAS* 88: 7185). More specifically, random PEGylation of antibody molecules has been described at lysine residues and thiolated derivatives (Ling and Mattiasson (1983) *Immunol. Methods* 59: 327; Wilkinson et al. (1987) *Immunol. Letters*, 15: 17; Kitamura et al. (1991) *Cancer Res.*

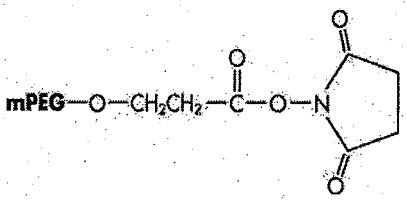
51: 4310; Delgado et al. (1996) *Br. J. Cancer*, 73: 175; Pedley et al. (1994) *Br. J. Cancer*, 70: 1126)

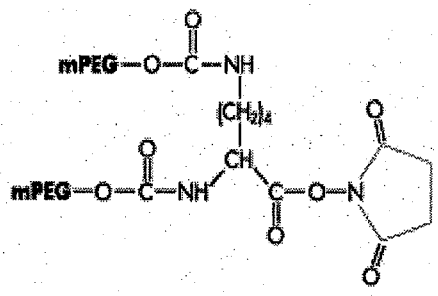
Accordingly, domain antibodies according to this aspect can be coupled, using methods known in the art to polymer molecules (in an aspect, PEG) useful for achieving the increased half-life and degradation resistance properties encompassed herein. Polymer moieties which can be utilized can be synthetic or naturally occurring and include, but are not limited to straight or branched chain polyalkylene, polyalkenylene or polyoxyalkylene polymers, or a branched or unbranched polysaccharide such as a homo- or heteropolysaccharide. Examples of synthetic polymers which may be used include straight or branched chain poly(ethylene glycol) (PEG), poly(propylene glycol), or poly(vinyl alcohol) and derivatives or substituted forms thereof. Useful substituted polymers include substituted PEG, including methoxy(polyethylene glycol). Naturally occurring polymer moieties which may be used herein in addition to or in place of PEG include lactose, amylose, dextran, or glycogen, as well as derivatives thereof which would be recognized by one of skill in the art. Derivatized forms of polymer molecules as set forth herein include, for example, derivatives which have additional moieties or reactive groups present therein to permit interaction with amino acid residues of the domain antibodies described herein. Such derivatives include N-hydroxylsuccinimide (NHS) active esters, succinimidyl propionate polymers, and sulfhydryl-selective reactive agents such as maleimide, vinyl sulfone, and thiol. Derivatized polymers include, but are not limited to PEG polymers having the formulae: PEG-O-$CH_2CH_2CH_2$-CO_2-NHS; PEG-O-CH_2-NHS; PEG-O-CH_2CH_2-CO_2-NHS; PEG-S-CH_2CH_2-CO-NHS; PEG-O_2CNH-CH(R)-CO_2-NHS; PEG-NHCO-CH_2CH_2-CO-NHS; and PEG-O-CH_2-CO_2-NHS; where R is $(CH_2)_4$)$NHCO_2$(mPEG). PEG polymers useful as set forth herein may be linear molecules, or may be branched wherein multiple PEG moieties are present in a single polymer. Useful PEG derivatives include, but are not limited to, mPEG-MAL, mPEG2-MAL, mPEG-$(MAL)^2$, multi-arm PEG, mPEG-SPA, mPEG2-NHS, and mPEG2-$(MAL)^2$, illustrated below:

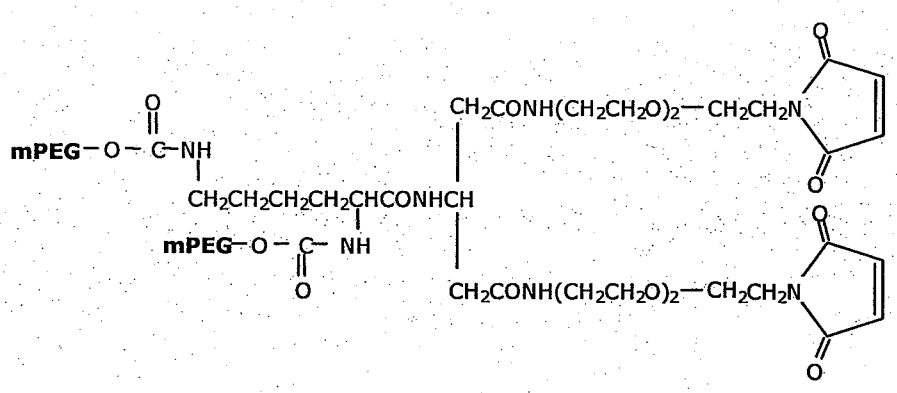












The reactive group (e.g., MAL, NHS, SPA, VS, or Thiol) may be attached directly to the PEG polymer or may be attached to PEG via a linker molecule.

The size of polymers useful as set forth herein can be in the range of between about 500 Da to 60 kD, for example, between about 1000 Da and 60 kD, 10 kD and 60 kD, 20 kD and 60 kD, 30 kD and 60 kD, 40 kD and 60 kD, and up to between 50 kD and 60 kD. The polymers used herein, particularly PEG, can be straight chain polymers or can possess a branched conformation. Depending on the combination of molecular weight and conformation, the polymer molecules useful as set forth herein, when attached

to a domain antibody, will yield a molecule having an average hydrodynamic size of between about 24 and 500 kD. The hydrodynamic size of a polymer molecule used herein refers to the apparent size of a molecule (e.g., a protein molecule) based on the diffusion of the molecule through an aqueous solution. The diffusion, or motion of a protein through solution can be processed to derive an apparent size of the protein, where the size is given by the Stokes radius or hydrodynamic radius of the protein particle. The "hydrodynamic size" of a protein depends on both mass and shape (conformation), such that two proteins having the same molecular mass may have differing hydrodynamic sizes based on the overall conformation of the protein. The hydrodynamic size of a PEG-linked domain antibody, e.g., a domain antibody as described herein, can be in the range of about 24 kD to 500 kD; 30 to 500 kD; 40 to 500 kD; 50 to 500 kD; 100 to 500 kD; 150 to 500 kD; 200 to 500 kD; 250 to 500 kD; 300 to 500 kD; 350 to 500 kD; 400 to 500 kD, and 450 to 500 kD. In an exemplary embodiment, the hydrodynamic size of a PEGylated domain antibody as described herein is about 30 to 40 kD; 70 to 80 kD or 200 to 300 kD. The size of a polymer molecule attached to a domain antibody may thus be varied depending upon the desired application. For example, where the PEGylated domain antibody is intended to leave the circulation and enter into peripheral tissues, it is desirable to keep the size of the attached polymer low to facilitate extravazation from the blood stream. Alternatively, where it is desired to have the PEGylated domain antibody remain in the circulation for a longer period of time, a higher molecular weight polymer can be used (e.g., a 30 to 60 kD polymer).

The polymer (PEG) molecules useful as set forth herein can be attached to domain antibodies using methods that are well known in the art. The first step in the attachment of PEG or other polymer moieties to a domain antibody is the substitution of the hydroxyl end-groups of the PEG polymer by electrophile-containing functional groups. Particularly, PEG polymers are attached to either cysteine or lysine residues present in the domain antibody. The cysteine and lysine residues can be naturally occurring, or can be engineered into the domain antibody molecule. For example, cysteine residues can be recombinantly engineered at the C-terminus of domain antibodies, or residues at specific solvent accessible locations in the domain antibody can be substituted with cysteine or lysine. In one embodiment, a PEG moiety is attached to a cysteine residue which is present in the hinge region at the C-terminus of a domain antibody.

In another embodiment a PEG moiety or other polymer is attached to a cysteine or lysine residue which is either naturally occurring at or engineered into the N-terminus of a domain antibody as set forth herein. In a still further embodiment, a PEG moiety or other polymer is attached to a domain antibody as set forth herein at a cysteine or lysine residue (either naturally occurring or engineered) which is at least 2 residues away from (e.g., internal to) the C- and/or N-terminus of the domain antibody.

In one embodiment, the PEG polymer(s) is attached to one or more cysteine or lysine residues present in a framework region (FWs) and one or more heterologous CDRs of a domain antibody. CDRs and framework regions (e.g., CDR1-CDR3 and FW1-FW4) are those regions of domain antibody as defined in the Kabat database of Sequences of Proteins of Immunological Interest (Kabat et al. (1991) *Sequences of Immunological Interest*, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.). In one embodiment, a PEG polymer is linked to a cysteine or lysine residue in the V_H framework segment DP47, or the V_k framework segment DPK9. Cysteine and/or lysine residues of DP47 which may be linked to PEG disclosed herein include the cysteine at positions 22, or 96 and the lysine at positions 43, 65, 76, or 98 of SEQ ID NO: 641. Cysteine and/or lysine residues of DPK9 which may be linked to PEG disclosed herein include the cysteine residues at positions 23, or 88 and the lysine residues at positions 39, 42, 45, 103, or 107 of SEQ ID NO: 643. (The DPK9 sequence of SEQ ID NO:643 is 95 amino acids in length; however, it is understood in the art that residues 103 and 107 are provided by the sequence encoded by the J gene segment, when fused to the DPK9 sequence.) In addition, specific cysteine or lysine residues may be linked to PEG in the V_H canonical framework region DP38, or DP45.

In addition, specific solvent accessible sites in the domain antibody which are not naturally occurring cysteine or lysine residues may be mutated to a cysteine or lysine for attachment of a PEG polymer. Solvent accessible residues in any given domain antibody can be determined using methods known in the art such as analysis of the crystal structure of the domain antibody. For example, using the solved crystal structure of the V_H dAb HEL4 (SEQ ID NO:399; a domain antibody that binds hen egg lysozyme), the residues Gln-13, Pro-14, Gly-15, Pro-41, Gly-42, Lys-43, Asp-62, Lys-65, Arg-87, Ala-88, Glu-89, Gln-112, Leu-115, Thr-117, Ser-119, and Ser-120 have been identified as being solvent accessible, and disclosed herein would be attractive candidates for mutation to cysteine or lysine residues for the attachment of a PEG polymer. In addition, using the

solved crystal structure of the V_k dummy domain antibody (SEQ ID NO:400), the residues Val-15, Pro-40, Gly-41, Ser-56, Gly-57, Ser-60, Pro-80, Glu-81, Gln-100, Lys-107, and Arg-108 have been identified as being solvent accessible, and disclosed herein would be attractive candidates for mutation to cysteine or lysine residues for the attachment of a PEG polymer. In one embodiment as disclosed herein, a PEG polymer is linked to multiple solvent accessible cysteine or lysine residues, or to solvent accessible residues which have been mutated to a cysteine or lysine residue. Alternatively, only one solvent accessible residue is linked to PEG, either where the particular domain antibody only possesses one solvent accessible cysteine or lysine (or residue modified to a cysteine or lysine) or where a particular solvent accessible residue is selected from among several such residues for PEGylation.

Primary amino acid sequence of HEL4 (SEQ ID NO:399):

```
  1  EVQLLESGGG LVQPGGSLRL SCAASGFRIS DEDMGWVRQA PGKGLEWVSS
 51  IYGPSGSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCASAL
101  EPLSEPLGFW GQGTLVTVSS
```

Primary amino acid sequence of V_k dummy (SEQ ID NO:400):

```
  1  DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLNWYQQKP GKAPKLLIYA
 51  ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPNTFGQ
101  GTKVEIKR
```

Several PEG attachment schemes disclosed herein are provided by the company Nektar (SanCarlos, CA). For example, where attachment of PEG or other polymer to a lysine residue is desired, active esters of PEG polymers which have been derivatized with N-hydroxylsuccinimide, such as succinimidyl propionate may be used. Where attachment to a cysteine residue is intended, PEG polymers which have been derivatized with sulfhydryl-selective reagents such as maleimide, vinyl sulfone, or thiols may be used. Other examples of specific embodiments of PEG derivatives which may be used as disclosed herein to generate PEGylated antibodies can be found in the Nektar Catalog (available on the world wide web at nektar.com). In addition, several derivitized forms of PEG may be used as disclosed herein to facilitate attachment of the PEG polymer to a domain antibody. PEG derivatives disclosed herein include, but are not limited to PEG-succinimidyl succinate, urethane linked PEG, PEG phenylcarbonate, PEG succinimidyl carbonate, PEG-carboxymethyl azide, dimethylmaleic anhydride PEG, PEG dithiocarbonate derivatives, PEG-tresylates (2,2,2-trifluoroethanesolfonates), mPEG

imidoesters, and other as described in Zalipsky and Lee, (1992) ("Use of functionalized poly(ethylene glycol)s for modification of peptides" in *Poly(Ethylene Glycol) Chemistry: Biotechnical and Biomedical Applications*, J. Milton Harris, Ed., Plenum Press, NY).

In one embodiment disclosed herein, a domain antibody composition comprises a domain antibody and PEG polymer wherein the ratio of PEG polymer to domain antibody is a molar ratio of at least 0.25:1. In a further embodiment, the molar ratio of PEG polymer to domain antibody is 0.33:1 or greater. In a still further embodiment the molar ratio of PEG polymer to domain antibody is 0.5:1 or greater.

6. Modification of Domain Antibodies

6.1. Diversification of the Canonical Sequence

Having selected several known main-chain conformations or, in an aspect, a single known main-chain conformation, ligands disclosed herein or libraries for use herein can be constructed by varying the binding site of the molecule in order to generate a repertoire with structural and/or functional diversity. This means that variants are generated such that they possess sufficient diversity in their structure and/or in their function so that they are capable of providing a range of activities.

The desired diversity is typically generated by varying the selected molecule at one or more positions. The positions to be changed can be chosen at random or are in an aspect, selected. The variation can then be achieved either by randomization, during which the resident amino acid is replaced by any amino acid or analogue thereof, natural or synthetic, producing a very large number of variants or by replacing the resident amino acid with one or more of a defined subset of amino acids, producing a more limited number of variants.

Various methods have been reported for introducing such diversity. Error-prone PCR (Hawkins *et al.* (1992) *J. Mol. Biol.*, 226: 889), chemical mutagenesis (Deng *et al.* (1994) *J. Biol. Chem.*, 269: 9533) or bacterial mutator strains (Low *et al.* (1996) *J. Mol. Biol.*, 260: 359) can be used to introduce random mutations into the genes that encode the molecule. Methods for mutating selected positions are also well known in the art and include the use of mismatched oligonucleotides or degenerate oligonucleotides, with or without the use of PCR. For example, several synthetic antibody libraries have been created by targeting mutations to the antigen binding loops. The H3 region of a human

tetanus toxoid-binding Fab has been randomized to create a range of new binding specificities (Barbas *et al.* (1992) *Proc. Natl. Acad. Sci. USA*, 89: 4457). Random or semi-random H3 and L3 regions have been appended to germline V gene segments to produce large libraries with unmutated framework regions (Hoogenboom & Winter (1992) *J. Mol. Biol.*, 227: 381; Barbas *et al.* (1992) *Proc. Natl. Acad. Sci. USA*, 89: 4457; Nissim *et al.* (1994) *EMBO J.*, 13: 692; Griffiths *et al.* (1994) *EMBO J.*, 13: 3245; De Kruif *et al.* (1995) *J. Mol. Biol.*, 248: 97). Such diversification has been extended to include some or all of the other antigen binding loops (Crameri *et al.* (1996) *Nature Med.*, 2: 100; Riechmann *et al.* (1995) *Bio/Technology*, 13: 475; Morphosys, WO97/08320, *supra*).

Since loop randomization has the potential to create approximately more than 10^{15} structures for H3 alone and a similarly large number of variants for the other five loops, it is not feasible using current transformation technology or even by using cell free systems to produce a library representing all possible combinations. For example, in one of the largest libraries constructed to date, 6×10^{10} different antibodies, which is only a fraction of the potential diversity for a library of this design, were generated (Griffiths *et al.* (1994) *supra*).

In one embodiment, only those residues which are directly involved in creating or modifying the desired function of the molecule are diversified. For many molecules, the function will be to bind a target and therefore diversity should be concentrated in the target binding site, while avoiding changing residues which are crucial to the overall packing of the molecule or to maintaining the chosen main-chain conformation.

6.1.1. Diversification of the Canonical Sequence As It Applies to Antibody Domains

In the case of the ligands disclosed herein, the binding site for the target is most often the antigen binding site. Thus, in one aspect, libraries of or for the assembly of antibody ligands in which only those residues in the antigen binding site are varied. These residues are extremely diverse in the human antibody repertoire and are known to make contacts in high-resolution antibody/antigen complexes. For example, in L2 it is known that positions 50 and 53 are diverse in naturally occurring antibodies and are observed to make contact with the antigen. In contrast, the conventional approach would have been to diversify all the residues in the corresponding Complementarity

Determining Region (CDR1) as defined by Kabat *et al.* (Kabat et al., 1991, Sequences of Immunological Interest, 5th ed. U.S. Dept. Health & Human Services, Washington, D.C.), some seven residues compared to the two diversified in the library for use as disclosed herein. This represents a significant improvement in terms of the functional diversity required to create a range of antigen binding specificities.

In nature, antibody diversity is the result of two processes: somatic recombination of germline V, D, and J gene segments to create a naive primary repertoire (so called germline and junctional diversity) and somatic hypermutation of the resulting rearranged V genes. Analysis of human antibody sequences has shown that diversity in the primary repertoire is focused at the centre of the antigen binding site whereas somatic hypermutation spreads diversity to regions at the periphery of the antigen binding site that are highly conserved in the primary repertoire (see Tomlinson *et al.* (1996) *J. Mol. Biol.*, 256: 813). This complementarity has probably evolved as an efficient strategy for searching sequence space and, although apparently unique to antibodies, it can easily be applied to other polypeptide repertoires. The residues which are varied are a subset of those that form the binding site for the target. Different (including overlapping) subsets of residues in the target binding site are diversified at different stages during selection, if desired.

In the case of an antibody repertoire, an initial 'naive' repertoire is created where some, but not all, of the residues in the antigen binding site are diversified. As used herein in this context, the term "naive" refers to antibody molecules that have no pre-determined target. These molecules resemble those which are encoded by the immunoglobulin genes of an individual who has not undergone immune diversification, as is the case with fetal and newborn individuals, whose immune systems have not yet been challenged by a wide variety of antigenic stimuli. This repertoire is then selected against a range of antigens or epitopes. If required, further diversity can then be introduced outside the region diversified in the initial repertoire. This matured repertoire can be selected for modified function, specificity or affinity.

Disclosed herein are two different naive repertoires of binding domains for the construction of ligands, or a naïve library of ligands, in which some or all of the residues in the antigen binding site are varied. The "primary" library mimics the natural primary repertoire, with diversity restricted to residues at the centre of the antigen binding site that are diverse in the germline V gene segments (germline diversity) or diversified

during the recombination process (junctional diversity). Those residues which are diversified include, but are not limited to, H50, H52, H52a, H53, H55, H56, H58, H95, H96, H97, H98, L50, L53, L91, L92, L93, L94, and L96. In the "somatic" library, diversity is restricted to residues that are diversified during the recombination process (junctional diversity) or are highly somatically mutated). Those residues which are diversified include, but are not limited to: H31, H33, H35, H95, H96, H97, H98, L30, L31, L32, L34, and L96. All the residues listed above as suitable for diversification in these libraries are known to make contacts in one or more antibody-antigen complexes. Since in both libraries, not all of the residues in the antigen binding site are varied, additional diversity is incorporated during selection by varying the remaining residues, if it is desired to do so. It shall be apparent to one skilled in the art that any subset of any of these residues (or additional residues which comprise the antigen binding site) can be used for the initial and/or subsequent diversification of the antigen binding site.

In the construction of libraries for use as disclosed herein, diversification of chosen positions is typically achieved at the nucleic acid level, by altering the coding sequence which specifies the sequence of the polypeptide such that a number of possible amino acids (all 20 or a subset thereof) can be incorporated at that position. Using the IUPAC nomenclature, the most versatile codon is NNK, which encodes all amino acids as well as the TAG stop codon. The NNK codon is, in an aspect, used in order to introduce the required diversity. Other codons which achieve the same ends are also of use, including the NNN codon, which leads to the production of the additional stop codons TGA and TAA.

A feature of side-chain diversity in the antigen binding site of human antibodies is a pronounced bias which favours certain amino acid residues. If the amino acid composition of the ten most diverse positions in each of the V_H, V_K, and V_λ regions are summed, more than 76% of the side-chain diversity comes from only seven different residues, these being, serine (24%), tyrosine (14%), asparagine (11%), glycine (9%), alanine (7%), aspartate (6%), and threonine (6%). This bias towards hydrophilic residues and small residues which can provide main-chain flexibility probably reflects the evolution of surfaces which are predisposed to binding a wide range of antigens or epitopes and may help to explain the required promiscuity of antibodies in the primary repertoire.

Since it is preferable to mimic this distribution of amino acids, the distribution of amino acids at the positions to be varied, in an aspect, mimics that seen in the antigen binding site of antibodies. Such bias in the substitution of amino acids that permits selection of certain polypeptides (not just domain antibodies) against a range of target antigens is easily applied to any polypeptide repertoire. There are various methods for biasing the amino acid distribution at the position to be varied (including the use of tri-nucleotide mutagenesis, see WO 97/08320), of which one advantageous method, due to ease of synthesis, is the use of conventional degenerate codons. By comparing the amino acid profile encoded by all combinations of degenerate codons (with single, double, triple, and quadruple degeneracy in equal ratios at each position) with the natural amino acid use it is possible to calculate the most representative codon. The codons (AGT)(AGC)T, (AGT)(AGC)C, and (AGT)(AGC)(CT) are those closest to the desired amino acid profile: they encode 22% serine and 11% tyrosine, asparagine, glycine, alanine, aspartate, threonine, and cysteine, and in an aspect, these codons are used in the construction of a library.

6.2. Dual-Specific Ligands

Also provided herein are dual-specific ligands comprising domain antibodies which each have respective specificities; that is, the first and the second epitopes bound by the dual-specific ligand are, in an aspect, different or are two copies of the same epitopes, the epitopes being bound by a respective variable domain. In an embodiment, a "dual-specific ligand" refers to a ligand comprising a first domain antibody and a second domain antibody as herein defined, wherein the variable regions are capable of binding to two different antigens or two epitopes on the same antigen which are not normally bound by a monospecific immunoglobulin. In another embodiment, a "dual-specific ligand" refers to a ligand comprising a domain antibody and an immunoglobulin variable domain as herein defined, wherein the variable regions are capable of binding to two different antigens or two epitopes on the same antigen which are not normally bound by a monospecific immunoglobulin. For example, the two epitopes may be on the same hapten, but are not the same epitope or sufficiently adjacent to be bound by a monospecific ligand. The dual specific ligands disclosed herein are composed of variable domains which have different specificities, and do not contain mutually complementary variable domain pairs which have the same specificity. Dual-specific ligands may be, or

be part of, polypeptides, proteins, or nucleic acids, which may be naturally occurring or synthetic.

Advantageously, the dual- or multispecific ligand may comprise a first domain capable of binding a target molecule, and a second domain capable of binding a molecule or group which extends the half-life of the ligand. For example, the molecule or group may be a bulky agent, such as HSA or a cell matrix protein. As used herein, the phrase "molecule or group which extends the half-life of a ligand" refers to a molecule or chemical group which, when bound by a dual-specific ligand as described herein increases the *in vivo* half-life of such dual specific ligand when administered to an animal, relative to a ligand that does not bind that molecule or group. Examples of molecules or groups that extend the half-life of a ligand are described herein below. In one embodiment, the closed conformation multispecific ligand may be capable of binding the target molecule only on displacement of the half-life enhancing molecule or group. Thus, for example, a closed conformation multispecific ligand is maintained in circulation in the bloodstream of a subject by a bulky molecule such as HSA. When a target molecule is encountered, competition between the binding domains of the closed conformation multispecific ligand results in displacement of the HSA and binding of the target. Molecules which increase half-life are discussed in further detail above.

In one embodiment of the second configuration disclosed herein, the variable domains are derived from an antibody directed against the first and/or second antigen or epitope. In one embodiment the variable domains are derived from a repertoire of single variable antibody domains. In one example, the repertoire is a repertoire that is not created in an animal or a synthetic repertoire. In another example, the single variable domains are not isolated (at least in part) by animal immunization. Thus, the single domains can be isolated from a naïve library.

In another aspect, disclosed herein is a multi-specific ligand comprising a first epitope binding domain having a first epitope binding specificity and a non-complementary second epitope binding domain having a second epitope binding specificity. The first and second binding specificities may be the same or different.

In a further aspect, disclosed herein is a closed conformation multi-specific ligand comprising a first epitope binding domain having a first epitope binding specificity and a non-complementary second epitope binding domain having a second epitope binding

specificity wherein the first and second binding specificities are capable of competing for epitope binding such that the closed conformation multi-specific ligand cannot bind both epitopes simultaneously.

Ligands according to any aspect as disclosed herein, as well as domain antibody monomers useful in constructing such ligands, may advantageously dissociate from their cognate target(s) with a K_d of about 300 nM to 1p M or 5 pM (ie, 3×10^{-7} to 5×10^{-12} M), in an aspect, about 50 nM to20 pM, or 5 nM to 200 pM or 1 nM to 100 pM, 1×10^{-7} M or less, 1×10^{-8} M or less, 1×10^{-9} M or less, 1×10^{-10} M or less, 1×10^{-11} M or less; and/or a K_{off} rate constant of about 5×10^{-1} to 1×10^{-7} S^{-1}, in an aspect, about 1×10^{-2} to 1×10^{-6} S^{-1}, or 5×10^{-3} to 1×10^{-5} S^{-1}, or 5×10^{-1} S^{-1} or less, or 1×10^{-2} S^{-1} or less, or 1×10^{-3} S^{-1} or less, or 1×10^{-4} S^{-1} or less, or 1×10^{-5} S^{-1} or less, or 1×10^{-6} S^{-1} or less as determined by surface plasmon resonance. The K_d rate constant is defined as K_{off}/K_{on}. Additional details regarding dual specific ligands can be found in WO 03/002609, WO 04/003019 and WO 04/058821.

Furthermore, a domain antibody monomer is provided (or dual specific ligand comprising such a domain antibody) that binds to serum albumin (SA) with a K_d of 1 nM to 500 μM (i.e., 1×10^{-9} M to 5×10^{-4} M), in an aspect, 100 nM to 10 μM. In an aspect, for a dual specific ligand comprising a first anti-SA domain antibody and a second domain antibody to another target, the affinity (e.g. K_d and/or K_{off} as measured by surface plasmon resonance, e.g. using BiaCore) of the second dAb for its target is from 1 to 100,000 times (in an aspect, 100 to 100,000, in a further aspect, 1000 to 100000, or 10000 to 100000 times) the affinity of the first domain antibody for SA. For example, the first domain antibody binds SA with an affinity of approximately 10 μM, while the second domain antibody binds its target with an affinity of about 100 pM. In an exemplary embodiment, the serum albumin is human serum albumin (HSA).

In one embodiment, the first domain antibody (or a domain antibody monomer) binds SA (eg, HSA) with a K_d of approximately about 50 nM, in an aspect, about 70 nM, and in another aspect, about 100, 150, or 200 nM.

Also provided are dimers, trimers and polymers of the aforementioned domain antibody monomers, in accordance with the foregoing aspect.

Ligands disclosed herein, including domain antibody monomers, dimers and trimers, can be linked to an antibody Fc region, comprising one or both of C_H2 and C_H3

domains, and optionally a hinge region. For example, vectors encoding ligands linked as a single nucleotide sequence to an Fc region may be used to prepare such polypeptides. Alternatively, ligands disclosed herein may be free of an Fc domain.

In a further aspect is provided one or more nucleic acid molecules encoding at least a dual- or multispecific ligand as herein defined. In one embodiment, the ligand is a closed conformation ligand. In another embodiment, it is an open conformation ligand. The multispecific ligand may be encoded on a single nucleic acid molecule; alternatively, each epitope binding domain may be encoded by a separate nucleic acid molecule. Where the ligand is encoded by a single nucleic acid molecule, the domains may be expressed as a fusion polypeptide, or may be separately expressed and subsequently linked together, for example using chemical linking agents. Ligands expressed from separate nucleic acids will be linked together by appropriate means.

The nucleic acid may further encode a signal sequence for export of the polypeptides from a host cell upon expression and may be fused with a surface component of a filamentous bacteriophage particle (or other component of a selection display system) upon expression. Leader sequences, which may be used in bacterial expression and/or phage or phagemid display, include pelB, stII, ompA, phoA, bla, ompT and pelA.

In a further aspect of the second configuration as disclosed herein includes a vector comprising nucleic acid.

In a yet further aspect is provided a host cell transfected with a vector.

Expression from such a vector may be configured to produce, for example on the surface of a bacteriophage particle, epitope binding domains for selection. This allows selection of displayed domains and thus selection of "multispecific ligands" using the method as disclosed herein.

6.2.1. Structure of 'Dual-Specific Ligands'

As described above, an antibody is herein defined as an antibody or fragment (Fab, Fv, disulfide linked Fv, scFv, diabody) which comprises at least one heavy and a light chain variable domain, at least two heavy chain variable domains or at least two light chain variable domains. It may be at least partly derived from any species naturally producing an antibody, or created by recombinant DNA technology; whether isolated from serum, B-cells, hybridomas, transfectomas, yeast or bacteria).

In one embodiment, the dual-specific ligand comprises at least one single heavy chain variable domain of an antibody and one single light chain variable domain of an antibody, or two single heavy or light chain variable domains. For example, the ligand may comprise a V_H/V_L pair, a pair of V_H domains or a pair of V_L domains.

The first and the second variable domains of such a ligand may be on the same polypeptide chain. Alternatively they may be on separate polypeptide chains. In the case that they are on the same polypeptide chain they may be linked by a linker, which may be a peptide sequence, as described above.

The first and second variable domains may be covalently or non-covalently associated. In the case that they are covalently associated, the covalent bonds may be disulphide bonds.

In the case that the variable domains are selected from V-gene repertoires selected for instance using phage display technology as herein described, then these variable domains comprise a universal framework region, such that is they may be recognized by a specific generic ligand as herein defined. The use of universal frameworks, generic ligands, and the like is described in WO 99/20749.

Where V-gene repertoires are used variation in polypeptide sequence is, in an aspect, located within the structural loops of the variable domains. The polypeptide sequences of either variable domain may be altered by DNA shuffling or by mutation in order to enhance the interaction of each variable domain with its complementary pair. DNA shuffling is known in the art and taught, for example, by Stemmer (1994) *Nature* 370: 389-391 and U.S. Patent No. 6,297,053, both of which are incorporated herein by reference. Other methods of mutagenesis are well known to those of skill in the art.

In one embodiment, the 'dual-specific ligand' is a single chain Fv fragment. In an alternative embodiment, the 'dual-specific ligand' consists of a Fab format.

A further aspect disclosed herein provides nucleic acid encoding at least a 'dual-specific ligand' as herein defined.

One skilled in the art will appreciate that, depending on the aspect, both antigens or epitopes may bind simultaneously to the same antibody molecule. Alternatively, they may compete for binding to the same antibody molecule. For example, where both epitopes are bound simultaneously, both variable domains of a dual specific ligand are able to independently bind their target epitopes. Where the domains compete, the one

variable domain is capable of binding its target, but not at the same time as the other variable domain binds its cognate target; or the first variable domain is capable of binding its target, but not at the same time as the second variable domain binds its cognate target.

The variable regions may be derived from antibodies directed against target antigens or epitopes. Alternatively they may be derived from a repertoire of single antibody domains such as those expressed on the surface of filamentous bacteriophage. Selection may be performed as described below.

In general, the nucleic acid molecules and vector constructs required for the performance as disclosed herein may be constructed and manipulated as set forth in standard laboratory manuals, such as Sambrook *et al.* (1989) *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor, USA.

The manipulation of nucleic acids useful as disclosed herein is typically carried out in recombinant vectors.

Thus, a further aspect disclosed herein provides a vector comprising nucleic acid encoding at least a 'dual-specific ligand' as herein defined.

As used herein, vector refers to a discrete element that is used to introduce heterologous DNA into cells for the expression and/or replication thereof. Methods by which to select or construct and, subsequently, use such vectors are well known to one of ordinary skill in the art. Numerous vectors are publicly available, including bacterial plasmids, bacteriophage, artificial chromosomes, and episomal vectors. Such vectors may be used for simple cloning and mutagenesis; alternatively gene expression vector is employed. A vector of use as disclosed herein may be selected to accommodate a polypeptide coding sequence of a desired size, typically from 0.25 kilobase (kb) to 40 kb or more in length. A suitable host cell is transformed with the vector after *in vitro* cloning manipulations. Each vector contains various functional components, which generally include a cloning (or "polylinker") site, an origin of replication, and at least one selectable marker gene. If given vector is an expression vector, it additionally possesses one or more of the following: enhancer element, promoter, transcription termination, and signal sequences, each positioned in the vicinity of the cloning site, such that they are operatively linked to the gene encoding a ligand as disclosed herein.

Both cloning and expression vectors generally contain nucleic acid sequences that enable the vector to replicate in one or more selected host cells. Typically in cloning

vectors, this sequence is one that enables the vector to replicate independently of the host chromosomal DNA and includes origins of replication or autonomously replicating sequences. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 micron plasmid origin is suitable for yeast, and various viral origins (e.g. SV 40, adenovirus) are useful for cloning vectors in mammalian cells. Generally, the origin of replication is not needed for mammalian expression vectors unless these are used in mammalian cells able to replicate high levels of DNA, such as COS cells.

Advantageously, a cloning or expression vector may contain a selection gene also referred to as selectable marker. This gene encodes a protein necessary for the survival or growth of transformed host cells grown in a selective culture medium. Host cells not transformed with the vector containing the selection gene will therefore not survive in the culture medium. Typical selection genes encode proteins that confer resistance to antibiotics and other toxins, e.g. ampicillin, neomycin, methotrexate or tetracycline, complement auxotrophic deficiencies, or supply critical nutrients not available in the growth media.

6.2.2. Combining Single Variable Domains

Domains useful as disclosed herein, once selected using methods exemplified above, may be combined by a variety of methods known in the art, including covalent and non-covalent methods.

Methods include the use of polypeptide linkers, as described, for example, in connection with scFv molecules (Bird *et al.*, (1988) *Science* 242: 423-426). Discussion of suitable linkers is provided in Bird *et al.*, *Science* 242: 423-426; Hudson *et al.*, (1999) *J. Immunol. Methods* 231: 177-189; Hudson *et al.*, *Proc. Nat'l Acad. Sci. USA* 85: 5879-5883. Linkers are in an aspect, flexible, allowing the two single domains to interact. One linker example is a $(Gly_4\ Ser)_n$ linker, where n=1 to 8, e.g., 2, 3, 4, 5, or 7. The linkers used in diabodies, which are less flexible, may also be employed (Holliger *et al.*, (1993) *PNAS* (USA) 90: 6444-6448).

In one embodiment, the linker employed is not an immunoglobulin hinge region.

Variable domains may be combined using methods other than linkers. For example, the use of disulphide bridges, provided through naturally-occurring or engineered cysteine residues, may be exploited to stabilize V_H-V_H, V_L-V_L or V_H-V_L

dimers (Reiter *et al.*, (1994) *Protein Eng.* 7: 697-704) or by remodeling the interface between the variable domains to improve the "fit" and thus the stability of interaction (Ridgeway *et al.*, (1996) *Protein Eng.* 7: 617-621; Zhu *et al.*, (1997) *Protein Science* 6: 781-788).

Other techniques for joining or stabilizing variable domains of immunoglobulins, and in particular antibody V_H domains, may be employed as appropriate.

As disclosed herein, dual specific ligands can be in "closed" conformations in solution. A "closed" configuration is that in which the two domains (for example V_H and V_L) are present in associated form, such as that of an associated V_H-V_L pair which forms an antibody binding site. For example, scFv may be in a closed conformation, depending on the arrangement of the linker used to link the V_H and V_L domains. If this is sufficiently flexible to allow the domains to associate, or rigidly holds them in the associated position, it is likely that the domains will adopt a closed conformation.

Similarly, V_H domain pairs and V_L domain pairs may exist in a closed conformation. Generally, this will be a function of close association of the domains, such as by a rigid linker, in the ligand molecule. Ligands in a closed conformation will be unable to bind both the molecule which increases the half-life of the ligand and a second target molecule. Thus, the ligand will typically only bind the second target molecule on dissociation from the molecule which increases the half-life of the ligand.

Moreover, the construction of V_H/V_H, V_L/V_L or V_H/V_L dimers without linkers provides for competition between the domains.

Ligands as disclosed herein may moreover be in an open conformation. In such a conformation, the ligands will be able to simultaneously bind both the molecule which increases the half-life of the ligand and the second target molecule. Typically, variable domains in an open configuration are (in the case of V_H-V_L pairs) held far enough apart for the domains not to interact and form an antibody binding site and not to compete for binding to their respective epitopes. In the case of V_H/V_H or V_L/V_L dimers, the domains are not forced together by rigid linkers. Naturally, such domain pairings will not compete for antigen binding or form an antibody binding site.

Fab fragments and whole antibodies will exist primarily in the closed conformation, although it will be appreciated that open and closed dual specific ligands are likely to exist in a variety of equilibria under different circumstances. Binding of the

ligand to a target is likely to shift the balance of the equilibrium towards the open configuration. Thus, certain ligands disclosed herein can exist in two conformations in solution, one of which (the open form) can bind two antigens or epitopes independently, whilst the alternative conformation (the closed form) can only bind one antigen or epitope; antigens or epitopes thus compete for binding to the ligand in this conformation.

Although the open form of the dual specific ligand may thus exist in equilibrium with the closed form in solution, it is envisaged that the equilibrium will favor the closed form; moreover, the open form can be sequestered by target binding into a closed conformation. In an exemplary embodiment, therefore, certain dual specific ligands disclosed herein are present in an equilibrium between two (open and closed) conformations.

Dual specific ligands disclosed herein may be modified in order to favor an open or closed conformation. For example, stabilization of V_H-V_L interactions with disulphide bonds stabilizes the closed conformation. Moreover, linkers used to join the domains, including V_H domain and V_L domain pairs, may be constructed such that the open from is favored; for example, the linkers may sterically hinder the association of the domains, such as by incorporation of large amino acid residues in opportune locations, or the designing of a suitable rigid structure which will keep the domains physically spaced apart.

6.2.3. Characterization of the Dual-Specific Ligand.

The binding of the dual-specific ligand to its specific antigens or epitopes can be tested by methods which will be familiar to those skilled in the art and include ELISA. In one embodiment, binding is tested using monoclonal phage ELISA.

Phage ELISA may be performed according to any suitable procedure: an exemplary protocol is set forth below.

Populations of phage produced at each round of selection can be screened for binding by ELISA to the selected antigen or epitope, to identify "polyclonal" phage antibodies. Phage from single infected bacterial colonies from these populations can then be screened by ELISA to identify "monoclonal" phage antibodies. It is also desirable to screen soluble antibody fragments for binding to antigen or epitope, and this can also be undertaken by ELISA using reagents, for example, against a C- or N-terminal tag (see for

example Winter *et al.* (1994) Ann. Rev. Immunology 12, 433-55 and references cited therein.

The diversity of the selected phage monoclonal antibodies may also be assessed by gel electrophoresis of PCR products (Marks *et al.* (1991) *supra*; Nissim *et al.* (1994) *supra*), probing (Tomlinson *et al.*, (1992) *J. Mol. Biol.* 227, 776) or by sequencing of the vector DNA.

7. Increasing Polypeptide Stability

7.1. Increasing Half-Life

In vivo, the PEGylated domain antibodies as described herein may confer a distinct advantage over non-PEGylated domain antibodies, in that the PEGylated antibody molecules will have a greatly prolonged *in vivo* half-life. It will be understood, in the context of the present disclosure, that a particular half-life of any composition may be either increased or decreased by the route of administration of the composition to a patient.

Nonetheless, without being bound to one particular theory, it is believed that the increased half-life of the molecules described herein is conferred by the increased hydrodynamic size of the domain antibody resulting from the attachment of PEG polymer(s). More specifically, it is believed that two parameters play an important role in determining the serum half-life of PEGylated domain antibodies. The first criterion is the nature and size of the PEG attachment, i.e., if the polymer used is simply a linear chain or a branched/forked chain, wherein the branched/forked chain gives rise to a longer half-life. The second is the location of the PEG moiety or moieties on the domain antibody in the final format and how many "free" unmodified PEG arms the molecule has. The resulting hydrodynamic size of the PEGylated domain antibody, as estimated, for example, by size exclusion chromatography, reflects the serum half-life of the molecule. Accordingly, the larger the hydrodynamic size of the PEGylated molecule, the greater the serum half-life.

Increased half-life is useful *in vivo* applications of immunoglobulins, especially antibodies and most especially antibody fragments of small size, as well as domain antibodies. Such fragments (Fvs, Fabs, scFvs) and domain antibodies suffer from rapid clearance from the body; thus, while they are able to reach most parts of the body rapidly,

and are quick to produce and easier to handle, their *in vivo* applications have been limited by their only brief persistence *in vivo*.

In one aspect, a domain antibody as described herein is stabilized *in vivo* by fusion with a moiety, such as PEG, that increases the hydrodynamic size of the domain antibody. Methods for pharmacokinetic analysis and determination of half-life will be familiar to those skilled in the art. Details may be found in Kenneth et al., *Chemical Stability of Pharmaceuticals: A Handbook for Pharmacists* and in Peters et al., *Pharmacokinetc Analysis: A Practical Approach* (1996). Reference is also made to "Pharmacokinetics", M. Gibaldi & D. Perron, published by Marcel Dekker, 2nd Rev. edition (1982), which describes pharmacokinetic parameters such as t-α and t-β half lives and area under the curve (AUC).

Typically, the half-life of a PEGylated domain antibody as described herein is increased by about 10%, 20%, 30%, 40%, 50%, or more relative to a non-PEGylated dAb (wherein the domain antibody of the PEGylated domain antibody and non-PEGylated domain antibody are the same). Increases in the range of 2x, 3x, 4x, 5x, 7x, 10x, 20x, 30x, 40x, and up to 50x or more of the half-life are possible. Alternatively, or in addition, increases in the range of up to 30x, 40x, 50x, 60x, 70x, 80x, 90x, 100x, or 150x of the half-life are possible.

Half lives (t½-α and t½-β) and AUC can be determined from a curve of serum concentration of ligand against time. The WinNonlin analysis package (available from Pharsight Corp., Mountain View, CA 94040, USA) can be used, for example, to model the curve. In a first phase (the alpha phase) the ligand is undergoing mainly distribution in the patient, with some elimination. A second phase (beta phase) is the terminal phase when the ligand has been distributed and the serum concentration is decreasing as the ligand is cleared from the patient. The "tα half-life" is the half-life of the first phase and the "tβ half-life" is the half-life of the second phase. "Half-life" as used herein, unless otherwise noted, refers to the overall half-life of an antibody single variable domain disclosed herein determined by non-compartment modeling (as contrasted with biphasic modeling, for example). Beta half-life is a measurement of the time it takes for the amount of domain antibody monomer or multimer to be cleared from the mammal to which it is administered. Thus, advantageously, a domain antibody-containing composition, e.g., a domain antibody-effector group composition is contemplated having

a tα half-life in the range of about 0.25 hours to 6 hours or more. In one embodiment, the lower end of the range is about 30 minutes, 45 minutes, 1 hour, 1.3 hours, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 10 hours, 11 hours, or 12 hours. In addition or alternatively, a domain antibody-containing composition will have a tα half-life in the range of up to and including 12 hours. In one embodiment, the upper end of the range is about 11, 10, 9, 8, 7, 6, or 5 hours. An example of a suitable range is about 1.3 to 6 hours, 2 to 5 hours, or 3 to 4 hours.

Advantageously, a domain antibody-containing composition comprising a ligand has a tβ half-life in the range of about 1-170 hours or more. In one embodiment, the lower end of the range is about 2.5 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, or 12 hours. In addition, or alternatively, a domain antibody-containing composition, e.g. a dAb-effector group composition has a tβ half-life in the range of up to and including 21 days. In one embodiment, the upper end of the range is about 12 hours, 24 hours, 2 days, 3 days, 5 days, 10 days, 15 days, or 20 days. Advantageously, a dAb containing composition disclosed herein will have a tβ half-life in the range about 2-100 hours, 4-80 hours, and 10-40 hours. In a further embodiment, it will be in the range of about 12-48 hours. In a further embodiment still, it will be in the range of about 12-26 hours. Disclosed herein is a domain antibody-containing composition comprising a ligand having a half-life in the range of 1-170 hours or more. In one embodiment, the lower end of the range is about 1.3 hours, 2.5 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, or 12 hours. In addition, or alternatively, a domain antibody-containing composition, e.g. a dAb-effector group composition, has a half-life in the range of up to and including 21 days. In one embodiment, the upper end of the range is about 12 hours, 24 hours, 2 days, 3 days, 5 days, 10 days, 15 days, or 20 days.

In addition, or alternatively to the above criteria, a domain antibody-containing composition comprising a ligand has an AUC value (area under the curve) in the range of 1 mg·min/ml or more. In one embodiment, the lower end of the range is about 5, 10, 15, 20, 30, 100, 200, or 300 mg·min/ml. In addition, or alternatively, a ligand or composition disclosed herein has an AUC in the range of up to about 600 mg·min/ml. In one embodiment, the upper end of the range is about 500, 400, 300, 200, 150, 100, 75, or 50 mg·min/ml. Exemplary ligands disclosed herein will have an AUC in the range selected

from the group consisting of the following: about 15 to 150 mg·min/ml, 15 to 100 mg·min/ml, 15 to 75 mg·min/ml, and 15 to 50 mg·.min/ml.

The ligands disclosed herein, including, mono-, dual- and multi-specific, in one configuration thereof, are capable of binding to one or more molecules which can increase the half-life of the ligand *in vivo*. Typically, such molecules are polypeptides which occur naturally *in vivo* and which resist degradation or removal by endogenous mechanisms which remove unwanted material from the organism.

For example, the molecule which increases the half-life in the organism may be selected from the following:

- Proteins from the extracellular matrix; for example collagen, laminins, integrins, and fibronectin. Collagens are the major proteins of the extracellular matrix. About 15 types of collagen molecules are currently known, found in different parts of the body, e.g. type I collagen (accounting for 90% of body collagen) found in bone, skin, tendon, ligaments, cornea, internal organs, or type II collagen found in cartilage, invertebral disc, notochord, vitreous humour of the eye.
- Proteins found in blood, including: Plasma proteins such as fibrin, α-2 macroglobulin, serum albumin, fibrinogen A, fibrinogen B, serum amyloid protein A, heptaglobin, profilin, ubiquitin, uteroglobulin, and β-2-microglobulin;
- Enzymes and inhibitors such as plasminogen, lysozyme, cystatin C, alpha-1-antitrypsin, and pancreatic trypsin inhibitor. Plasminogen is the inactive precursor of the trypsin-like serine protease plasmin. It is normally found circulating through the blood stream. When plasminogen becomes activated and is converted to plasmin, it unfolds a potent enzymatic domain that dissolves the fibrinogen fibers that entangle the blood cells in a blood clot. This is called fibrinolysis.
- Immune system proteins, such as IgE, IgG, and IgM.
- Transport proteins such as retinol binding protein, α-1 microglobulin.
- Defensins such as beta-defensin 1, neutrophil defensins 1, 2, and 3.
- Proteins found at the blood brain barrier or in neural tissues, such as melanocortin receptor, myelin, ascorbate transporter.

- Transferrin receptor specific ligand-neuropharmaceutical agent fusion proteins (*see* U.S. Patent No. 5,977,307); brain capillary endothelial cell receptor, transferrin, transferrin receptor, insulin, insulin-like growth factor 1 (IGF 1) receptor, insulin-like growth factor 2 (IGF 2) receptor, insulin receptor.
- Proteins localised to the kidney, such as polycystin, type IV collagen, organic anion transporter K1, Heymann's antigen.
- Proteins localised to the liver, for example alcohol dehydrogenase, G250.
- Blood coagulation factor X
- α1 antitrypsin
- HNF 1α
- Proteins localised to the lung, such as secretory component (binds IgA).
- Proteins localised to the heart, for example HSP 27. This is associated with dilated cardiomyopathy.
- Proteins localised to the skin, for example keratin.
- Bone specific proteins, such as bone morphogenic proteins (BMPs), which are a subset of the transforming growth factor β superfamily that demonstrate osteogenic activity. Examples include BMP-2, -4, -5, -6, -7 (also referred to as osteogenic protein (OP-1) and -8 (OP-2).
- Tumour specific proteins, including human trophoblast antigen, herceptin receptor, oestrogen receptor, cathepsins (e.g. cathepsin B) (found in liver and spleen).
- Disease-specific proteins, such as antigens expressed only on activated T cells: including LAG-3 (lymphocyte activation gene), osteoprotegerin ligand (OPGL) (*see Nature* 402, 304–309; 1999); OX40 (a member of the TNF receptor family, expressed on activated T cells and the only co-stimulatory T cell molecule known to be specifically up-regulated in human T cell leukemia virus type-I (HTLV-I)-producing cells.) (*see J. Immunol.* 165(1): 263-70, 2000); metalloproteases (associated with arthritis/cancers), including CG6512 Drosophila, human paraplegin, human FtsH, human AFG3L2, murine ftsH; angiogenic growth factors, including acidic fibroblast growth factor (FGF-1), basic fibroblast growth

factor (FGF-2), vascular endothelial growth factor / vascular permeability factor (VEGF/VPF), transforming growth factor-a (TGF a), tumor necrosis factor-alpha (TNF-α), angiogenin, interleukin-3 (IL-3), interleukin-8 (IL-8), platelet-derived endothelial growth factor (PD-ECGF), placental growth factor (PlGF), midkine platelet-derived growth factor-BB (PDGF), fractalkine.

- Stress proteins (heat shock proteins). HSPs are normally found intracellularly. When they are found extracellularly, it is an indicator that a cell has died and spilled out its contents. This unprogrammed cell death (necrosis) only occurs when as a result of trauma, disease, or injury, and therefore *in vivo*, extracellular HSPs trigger a response from the immune system that will fight infection and disease. A dual specific which binds to extracellular HSP can be localized to a disease site.

- Proteins involved in Fc transport, such as:

  - The Brambell receptor (also known as FcRB). This Fc receptor has two functions, both of which are potentially useful for delivery. The functions include the transport of IgG from mother to child across the placenta and the protection of IgG from degradation thereby prolonging its serum half-life of IgG. It is thought that the receptor recycles IgG from endosome (*see* Holliger *et al*, (1997) *Nat. Biotechnol.* 15: 632-6).

  - Other proteins involved in Fc transport include the neonatal Fc receptor (FcRn) described in Gastinel et al. (1992) *PNAS* 89: 638; and Roopenian et al. (2003) *J. Immunol.* 170: 3528.

- Ligands disclosed herein may be designed to be specific for the above targets without requiring any increase in or increasing half-life *in vivo*. For example, ligands disclosed herein can be specific for targets selected from the foregoing which are tissue-specific, thereby enabling tissue-specific targeting of the dual specific ligand, or a domain antibody that binds a tissue-specific therapeutically relevant target, irrespective of any increase in half-life, although this may result. Moreover, where the ligand or domain antibody targets kidney or liver, this may redirect the ligand or domain antibody to an alternative clearance pathway *in vivo* (for example, the ligand may be directed away from liver clearance to kidney clearance).

Polypeptides useful for increasing half-life include, but are not limited to those shown in Annex I.

7.2. Increasing Resistance to Protease Degradation

Also disclosed herein is that the PEGylated domain antibodies and domain antibody multimers described herein possess increased stability to the action of proteases. In the presence of pepsin many domain antibodies are totally degraded at pH 2 because the protein is unfolded under the acid conditions, thus making the protein more accessible to the protease enzyme. Provided herein are PEGylated domain antibody molecules, including domain antibody multimers, wherein it is believed that the PEG polymer provides protection of the polypeptide backbone due the physical coverage of the backbone by the PEG polymer, thereby preventing the protease from gaining access to the polypeptide backbone and cleaving it. In one embodiment a PEGylated domain antibody having a higher hydrodynamic size (e.g., 200 to 500 kD) is generated as disclosed herein, because the larger hydrodynamic size will confirm a greater level of protection from protease degradation than a PEGylated domain antibody having a lower hydrodynamic size. In one embodiment, a PEG- or other polymer-linked antibody single variable domain monomer or multimer is degraded by no more than 10% when exposed to one or more of pepsin, trypsin, elastase, chymotrypsin, or carboxypeptidase, wherein if the protease is pepsin then exposure is carried out at pH 2.0 for 30 minutes, and if the protease is one or more of trypsin, elastase, chymotrypsin, or carboxypeptidase, then exposure is carried out at pH 8.0 for 30 minutes. In one embodiment, a PEG- or other polymer-linked domain antibody monomer or multimer is degraded by no more than 10% when exposed to pepsin at pH 2.0 for 30 minutes, in an aspect, no more than 5%, and in another aspect, not degraded at all. In another embodiment, a PEG- or other polymer-linked domain antibody multimer (e.g., hetero- or homodimer, trimer, tetramer, octamer, etc.) disclosed herein is degraded by less than 5%, and is, in an aspect, not degraded at all in the presence of pepsin at pH 2.0 for 30 minutes. In an exemplary embodiment, a PEG- or other polymer-linked domain antibody monomer or multimer is degraded by no more than 10% when exposed to trypsin, elastase, chymotrypsin, or carboxypeptidase at pH 8.0 for 30 minutes, in an aspect, no more than 5%, and in a further aspect, not degraded at all. In a further exemplary embodiment, a PEG- or other polymer-linked domain antibody multimer (e.g., hetero- or homodimer, trimer, tetramer, octamer, etc.) disclosed herein is

degraded by less than 5%, and is, in an aspect, not degraded at all in the presence of trypsin, elastase, chymotrypsin, or carboxypeptidase at pH 8.0 for 30 minutes.

The relative ratios of protease : PEG-domain antibody may be altered as disclosed herein to achieve the desired level of degradation as described above. For example the ratio of protease to PEG-domain antibody may be from about 1:30, to about 10:40, to about 20:50, to about 30:50, about 40:50, about 50:50, about 50:40, about 50:30, about 50:20, about 50:10, about 50:1, about 40:1, and about 30:1.

Accordingly, disclosed herein is a method for decreasing the degradation of domain antibody comprising linking a domain antibody monomer or multimer to a PEG polymer according to any of the embodiments described herein. As disclosed herein, the domain antibody is degraded by no more than 10% in the presence of pepsin at pH 2.0 for 30 minutes. In particular, a PEG-linked dAb multimer is degraded by no more than 5%, and in an aspect, not degraded at all in the presence of pepsin at pH 2.0 for 30 minutes. In an alternate embodiment, the domain antibody is degraded by no more than 10% when exposed to trypsin, elastase, chymotrypsin, or carboxypeptidase at pH 8.0 for 30 minutes, in an aspect, no more than 5%, and in another aspect, not degraded at all.

Degradation of PEG-linked domain antibody monomers and multimers as set forth herein may be measured using methods which are well known to those of skill in the art. For example, following incubation of a PEG-linked domain antibody with pepsin at pH 2.0 for 30 minutes, or with trypsin, elastase, chymotrypsin, or carboxypeptidase at pH 8.0 for 30 minutes, the domain antibody samples may be analyzed by gel filtration, wherein degradation of the domain antibody monomer or multimer is evidenced by a gel band of a smaller molecular weight than an un-degraded (i.e., control domain antibody not treated with pepsin, trypsin, chymotrypsin, elastase, or carboxypeptidase) domain antibody. Molecular weight of the domain antibody bands on the gel may be determined by comparing the migration of the band with the migration of a molecular weight ladder (see FIG. 5). Other methods of measuring protein degradation are known in the art and may be adapted to evaluate the PEG-linked domain antibody monomers and multimers as disclosed herein.

8. Uses of Domain Antibodies

Domain antibodies as described herein are useful for antagonizing the activity of CD28. Therefore, domain antibodies as described herein can be used to treat a patient having a condition, disease or disorder mediated in whole or in part by CD28 activity.

Domain antibodies as described herein are useful for the treatment or prevention of diseases or disorders in which inappropriate activation of a CD28 -mediated pathway is involved. Domain antibodies as described herein are also useful for the treatment, prevention, or alleviation of symptoms of diseases or disorders in which inappropriate activation of a CD28-mediated pathway is involved.

In an aspect, autoimmune diseases frequently involve inappropriate regulation or activity of CD28 pathways. Administration of a domain antibody as described herein to an individual suffering from such a disease, including an autoimmune disease, can reduce one or more symptoms of the disease. Non-limiting examples of diseases for which the domain antibodies described herein can be therapeutically useful include, but are not limited to, Addison's disease, allergy, ankylosing spondylitis, asthma, atherosclerosis, autoimmune diseases of the ear, autoimmune diseases of the eye, autoimmune atrophic gastritis, autoimmune hepatitis, autoimmune hymolytic anemia, autoimmune parotitis, primary biliary cirrhosis, benign lymphocytic aniitis, colitis, coronary heart disease, Crohn's disease, diabetes (Type I), diabetes, including Type 1 and/or Type 2 diabetes, epididymitis, glomerulonephritis, Goodpasture's syndrome, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, hemolytic anemia, idiopathic thrombocytopenic purpura, inflammatory bowel disease (IBD), immune response to recombinant drug products, e.g., factor VII in hemophilia, systemic lupus erythematosus, lupus nephritis, male infertility, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, primary myxedema, pemphigus, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, spondyloarthropathies, sympathetic ophthalmia, T-cell lymphoma, T-cell acute lymphoblastic leukemia, testicular antiocentric T-cell lymphoma, thyroiditis, transplant rejection, ulcerative colitis, autoimmune uveitis, and vasculitis. Autoimmune-mediated conditions include, but are not limited to, conditions in which the tissue affected is the primary target, and in some cases, the secondary target. Such conditions include, but are not limited to, AIDS, atopic allergy, bronchial asthma, eczema, leprosy, schizophrenia, inherited depression, transplantation of tissues and organs, chronic fatigue

syndrome, Alzheimer's disease, Parkinson's disease, myocardial infarction, stroke, autism, epilepsy, Arthus's phenomenon, anaphylaxis, and alcohol and drug addiction.

The domain antibodies described herein also can be therapeutically useful in graft-related diseases, such as graft versus host disease (GVHD), acute transplantation rejection, and chronic transplantation rejection.

The domain antibodies described herein are additionally useful in the way that generally any antibody preparation is useful, e.g., for *in vivo* imaging or diagnostic uses, *in vitro* diagnostic uses, etc.

For these and other uses it may be desirable to label the domain antibodies, e.g., with a fluorescent, colorimetric, enzymatic or radioactive label. Methods of labeling domain antibodies are well known in the art.

9. Pharmaceutical Compositions, Dosage, and Administration

The domain antibodies set forth herein can be incorporated into pharmaceutical compositions suitable for administration to a subject. Typically, the pharmaceutical composition comprises a domain antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, antibacterial, and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible. The term "pharmaceutically acceptable carrier" excludes tissue culture medium comprising bovine or horse serum. Examples of pharmaceutically acceptable carriers include one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations thereof. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Pharmaceutically acceptable substances include minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives or buffers, which enhance the shelf life or effectiveness of the domain antibody.

The compositions as described herein may be in a variety of forms. These include, for example, liquid, semi-solid, and solid dosage forms, such as liquid solutions (e.g., injectable and infusible solutions), dispersions or suspensions, powders, liposomes, and suppositories. The preferred form depends on the intended mode of administration and therapeutic application. Typical preferred compositions are in the form of injectable or infusible solutions, such as compositions similar to those used for passive

immunization of humans with other antibodies. One mode of administration is parenteral (e.g., intravenous, subcutaneous, intraperitoneal, intramuscular).

Therapeutic compositions typically must be sterile and stable under the conditions of manufacture and storage. The composition can be formulated as a solution, microemulsion, dispersion, liposome, or other ordered structure suitable to high drug concentration. Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filter sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation include vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof. The proper fluidity of a solution can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants.

The domain antibodies described herein can be administered by a variety of methods known in the art, although for many therapeutic applications, the preferred route/mode of administration is intravenous injection or infusion. The polypeptide can also be administered by intramuscular or subcutaneous injection.

As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. In certain embodiments, the active compound may be prepared with a carrier that will protect the compound against rapid release, such as a controlled release formulation, including implants, and microencapsulated delivery systems. Domain antibodies are well suited for formulation as extended release preparations due, in part, to their small size, the number of moles per dose can be significantly higher than the dosage of, *e.g.*, full sized antibodies. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Prolonged absorption of injectable compositions can be brought about by including in the composition an agent that delays absorption, for example, monostearate salts and gelatin. Many methods for the preparation of such formulations are patented or generally known to those skilled in the art. *See, e.g., Sustained and Controlled Release Drug Delivery*

Systems, J. R. Robinson, ed., Marcel Dekker, Inc., New York, 1978. Additional methods applicable to the controlled or extended release of polypeptide agents such as the monovalent domain antibodies disclosed herein are described, for example, in U.S. Patent Nos. 6,306,406 and 6,346,274, as well as, for example, in U.S. Patent Publication Nos. US20020182254 and US20020051808, all of which are incorporated herein by reference for all purposes.

Additional active compounds can also be incorporated into the compositions. In certain embodiments, a domain antibody is co-formulated with and/or co-administered with one or more additional therapeutic agents. For example, a domain antibody can be co-formulated and/or co-administered with one or more additional antibodies that bind other targets (e.g., antibodies that bind other cytokines or that bind cell surface molecules), or, for example, one or more cytokines. Such combination therapies may utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications associated with the various monotherapies.

The pharmaceutical compositions disclosed herein can include a "therapeutically effective amount" or a "prophylactically effective amount" of a domain antibody. A "therapeutically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic result. A therapeutically effective amount of the domain antibody can vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of domain antibody to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the antibody or antibody portion are outweighed by the therapeutically beneficial effects. A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically, because a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

Dosage regimens may be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. It is advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers

to physically discrete units suited as unitary dosages for the mammalian subjects to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

A non-limiting range for a therapeutically or prophylactically effective amount of a domain antibody is 0.1-20 mg/kg, and in an aspect, 1-10 mg/kg. It is to be noted that dosage values can vary with the type and 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 administering clinician.

The efficacy of treatment with a domain antibody as described herein is judged by the skilled clinician on the basis of improvement in one or more symptoms or indicators of the disease state or disorder being treated. An improvement of at least 10% (increase or decrease, depending upon the indicator being measured) in one or more clinical indicators is considered "effective treatment," although greater improvements are included, such as about 20%, 30%, 40%, 50%, 75%, 90%, or even 100%, or, depending upon the indicator being measured, more than 100% (e.g., two-fold, three-fold, ten-fold, etc., up to and including attainment of a disease-free state. Indicators can be physical measurements, e.g., enzyme, cytokine, growth factor or metabolite levels, rate of cell growth or cell death, or the presence or amount of abnormal cells. One can also measure, for example, differences in the amount of time between flare-ups of symptoms of the disease or disorder (e.g., for remitting/relapsing diseases, such as multiple sclerosis). Alternatively, non-physical measurements, such as a reported reduction in pain or discomfort or other indicator of disease status can be relied upon to gauge the effectiveness of treatment. Where non-physical measurements are made, various clinically acceptable scales or indices can be used, for example, the Crohn's Disease Activity Index, or CDAI (Best et al. (1976) *Gastroenterology* 70: 439), which combines both physical indicators, such as hematocrit and the number of liquid or very soft stools, among others, with patient-reported factors such as the severity of abdominal pain or cramping and general well-being, to assign a disease score.

The efficacy of treatment for psoriasis, for example, can be monitored using the Salford Psoriasis Index (SPI) or Psoriasis Area Severity Index (PASI). The PASI is most commonly used method to assess psoriasis disease severity in clinical trials, although it

can be exceedingly cumbersome for use in daily clinical practice. The method involves the body being divided into four sections (Legs, which have 40% of a person's skin; the Body (trunk area: stomach, chest, back, etc.) with 30%; the Arms (20%); and the Head (10%)). Each of these areas is scored by itself, and then the four scores are combined into the final PASI. For each section, the percent of area of skin involved, is estimated and then transformed into a grade from 0 to 6:

0% of inwolved area, grade: 0
< 10% of involved area, grade: 1
10-29% of involved area, grade: 2
30-49% of involved area, grade: 3
50-69% of involved area, grade: 4
70-89% of involved area, grade: 5
90-100% of involved area, grade: 6

The severity is estimated by four different parameters: Itching, Erythema (redness), Scaling and Thickness (psoriatic skin is thicker than normal skin). Severity parameters are measured on a scale of 0 to 4, from none to maximum.

The sum of all four severity parameters is than calculated for each section of skin, multiplied by the area score for that area and multiplied by weight of respective section (0.1 for head, 0.2 for arms, 0.3 for body and 0.4 for legs). Example:
(Ihead+Ehead+Shead+Thead) x Ahead x 0.1 = Totalhead.

At the end the total PASI is calculated as a sum of PASIs for all four skin sections. Computer-aided measurement of psoriatic lesion area was found to improve the power of the clinical trial, compared to the standard approach. The physician's estimations of the psoriatic lesion area tend to overestimate. The adapted PASI index, where the psoriatic area was not converted into an area grade, but was maintained as a continuous variable, also improved the power of the clinical trial. The modified PASI which involves computer aided area measurement as a continuous variable is named: Computer aided psoriasis continuous area and severity score cPcASI.

The efficacy of treatment for organ transplant rejection can also be monitored. The survival rates of organ transplant patients (currently around 70-85% for 5 years for all transplanted organs) have improved as a result of advances in organ preservation and immunosuppressive treatments. However, organ rejection, especially the acute rejection

that occurs in the first few weeks following surgery, as well as chronic graft rejection, is still one of the major causes of functional failure in organ transplantation. Current diagnosis or confirmation of graft rejection following solid organ transplantation requires biopsy of the tissue in order to detect the infiltration of immune cells (e.g., T-cells, macrophages, etc.) into the graft and other pathological changes. Tissue biopsy is not only invasive, but it is associated with increased health risk to the patent and is prone to sampling errors that can lead to false negative results. Alternative non-invasive methods are being developed, such as magnetic resonance imaging (MRI) which can be used to monitor the accumulation of immune cells at the rejected organ (Ho et al., (2004) *Curr. Pharm. Biotech.*, 5: 551-566).

As the term is used herein, "prophylaxis" performed using a composition as described herein is "effective" if the onset or severity of one or more symptoms is delayed or reduced by at least 10%, or abolished, relative to such symptoms in a similar individual (human or animal model) not treated with the composition.

Whereas the domain antibodies described herein bind human CD28, where one is to evaluate its effect in an animal model system, the polypeptide must cross-react with one or more antigens in the animal model system, in an aspect, at high affinity. One of skill in the art can readily determine if this condition is satisfied for a given animal model system and a given domain antibody. If this condition is satisfied, the efficacy of the domain antibody can be examined by administering it to an animal model under conditions which mimic a disease state and monitoring one or more indicators of that disease state for at least a 10% improvement.

10. Animal Models

Domain antibodies as described herein are useful for the treatment of autoimmune disorders in which CD28 signaling is inappropriately active. There are several animal models in which the therapeutic efficacy of a given domain antibody can be assessed, as discussed below.

10.1. Inflammatory Bowel Disease (IBD) Model ($CD4^+$ $CD45RB^{high}$ to SCID or $Rag^{-/-}$ mice) - Chronic Model

An IBD model includes using the mucosal immunity and inflammation system discussed by De Winter et al. (1999) *Am. J. Physiol.* 276: G1317-1321. Briefly, IBD is a multifactorial immune disorder of uncertain etiology. Several mouse models of mucosal

inflammation that resemble IBD have provided insight into the mechanisms governing both normal and pathological mucosal immune function. In one aspect, the injection into immunodeficient mice of a subset of CD4(+) T lymphocytes, the CD4(+)CD45RBhigh cells, leads to inflammation of the intestine. Pathogenesis is due in part to the secretion of proinflammatory cytokines. In another aspect, the induction of colitis can be prevented by co-transfer of another CD4(+) subpopulation, the CD4(+)CD45RBlow T cells. This population behaves analogously to the CD4(+)CD45RBhigh population in terms of the acquisition of activation markers and homing to the host intestine. However, their lymphokine profile when activated is different, and anti-inflammatory cytokines secreted and/or induced by CD4(+)CD45RBlow T cells prevent colitis. De Winter et al. provide a description of the adoptive transfer model and the factors that promote and prevent colitis pathogenesis.

10.2. Spontaneous Arthritis Model in KRN TCR Tg Crossed with NOD Mice - Chronic Model

A model of organ-specific disease provoked by systemic autoimmunity is provided by Kouskoff et al. (1996) *Cell* 87: 811-822. Rheumatoid arthritis (RA) is a chronic joint disease characterized by leukocyte invasion and synoviocyte activation followed by cartilage and bone destruction. The etiology and pathogenesis of RA are poorly understood. Kouskoff et al. present a spontaneous mouse model of RA, generated by crossing a T cell receptor (TCR) transgenic line with the NOD strain. All offspring develop a joint disease highly reminiscent of RA in man. The trigger for the murine disorder is chance recognition of a NOD-derived major histocompatibility complex (MHC) class II molecule by the transgenic TCR; progression to arthritis involves CD4+ T, B, and probably myeloid cells.

10.3. Mouse Collagen Induced Arthritis - Chronic Model

A mouse model of collagen-induced arthritis is provided by Brand et al. (2004) *Methods Mol. Med.* 102: 295-312. Briefly, collagen-induced arthritis (CIA) is an experimental autoimmune disease that can be elicited in susceptible strains of rodents (rat and mouse) and non-human primates by immunization with type II collagen (CII), the major constituent protein of articular cartilage. After immunization, the animals develop an autoimmune polyarthritis that shares several clinical and histological features with RA. Susceptibility to CIA in rodents is linked to the class II molecules of the major

histocompatibility complex (MHC), and the immune response to CII is characterized by both the stimulation of collagen-specific T cells and the production of high titers of antibody specific for both the immunogen (heterologous CII) and the autoantigen (mouse CII). Histologically, murine CIA is characterized by an intense synovitis that corresponds precisely with the clinical onset of arthritis. This experimental data is useful evaluating CIA because of the pathological similarities between CIA and RA.

10.4. Antigen Induced T Cell Proliferation *in vivo* - Acute Model

The use of adoptive transfer of T-cell-antigen-receptor-transgenic T cell for the study of T-cell activation in vivo provides a model for antigen-induced T-cell proliferation. Pape et al., (1997) *Immunol. Rev.* 156: 67-78 discuss adoptive transfer of TCR-transgenic T cells uniformly expressing an identifiable TCR of known peptide/MHC specificity can be used to monitor the in vivo behavior of antigen-specific T cells. The system was used to demonstrate that naive T cells are initially activated within the T-cell zones of secondary lymphoid tissue to proliferate in a B7-dependent manner. If adjuvants or inflammatory cytokines are present during this period, enhanced numbers of T cells accumulate, migrate into B-cell-rich follicles, and acquire the capacity to produce IFN-gamma and help B cells produce IgG2a. If inflammation is absent, most of the initially activated antigen-specific T cells disappear without entering the follicles, and the survivors are poor producers of IL-2 and IFN-gamma.

EXAMPLES

Example 1: Selection of Binding Domain Antibodies

Selections of binding domain antibodies (dAbs) were carried out with recombinant human CD28/Fc Chimera (R&D Systems, Abingdon, UK). The domain antibody library used for selections was based on a single human VH framework (V3-23 aka DP47, and JH4b) and a single human VL framework (012/02 aka DPκ9, and Jκ1). The dAb genes were genetically linked to the fd phage gene III protein under the control of the GAS1 leader sequence in the pDOM4 vector (FIG. 1) which contained all the fd genes necessary to generate infective phage particles. The first round of phage selection was performed by premixing phage library (4 pools for the VH libraries [VH11-13, VH14-15, VH16-17, VH18-19] and a single pool for the VK library) with 2% MPBS (Phosphate Buffered Saline supplemented with 2% Marvel dried skim milk powder) and adding CD28-Fc (R&D Systems, UK) to a final concentration of 100 nM. The mixture

was incubated for at least 1 hour at room temperature with mixing end-over-end then the antigen-phage complexes captured using protein G Dynabeads (Dynal, Sweden) and washed 8 times with 1ml PBST (PBS supplemented with 0.1% Tween 20) followed by a singe wash in 1 ml PBS. The washed phage were eluted from the antigen/bead complex by incubating with 0.5 ml of 1 mg/ml trypsin Type XIII from Bovine Pancreas (Sigma Aldrich, UK) in PBS (supplemented with 5 mM Tris-HCl pH 7.4, 0.1 mM $CaCl_2$). Eluted phage were used to infect *E. coli* and the output phage titres were determined to be between $1x10^4$ to $1x10^5$ titer units (t.u.)/ml, wherein t.u./ml is a measure of infective phage particles per ml. A measure of t.u. is determined through the infection of *E. coli* with phage of a given dilution, followed by growth of infected *E. coli* on selective agar plates.

A second round of selection was performed using enriched phage recovered from the previous round of selection with a final concentration of 50nM CD28-Fc followed by capture using protein G beads as described above. Output titres were in the range $1x10^6$ to $1x10^9$ t.u./ml.

A third round of selection using 10 nM CD28-Fc followed by capture using protein G beads was performed. The eluted phage titres were in the range of $2x10^9$ to $8x10^9$ t.u./ml.

Monoclonal phage ELISAs were carried out following selection rounds 2 and 3. All washes were performed using 3 washes of 250 µl PBST followed by 3 washes of 250 µl PBS. Plates were coated overnight at 4°C with 1 mg/ml and 0.6 mg/ml CD28-Fc in PBS respectively. Plates were washed, then blocked with 2% MPBS for 1 hour at room temperature. The plates were washed and phage supernatants added to an equal volume of 2% MPBS and incubated for 1 hour at room temperature. The plates were washed and bound phage detected with anti-M13-HRP conjugate (GE Healthcare, UK) diluted 1:5000 in 2% MPBS and incubated for 1 hour at room temperature. The plates were washed and the ELISA developed using SureBlue 1-Component TMB MicroWell Peroxidase solution (KPL Inc, USA). Specific phage were identified by comparison with a plate coated with 1mg/ml Fc (Sigma Aldrich, UK). After round 2, specific phages were mainly identified in library pools VH14-15, VH18-19 and VK, whereas by round 3, few specific phage remained. All round 2 pools were subcloned into pDOM5 (FIG. 2) and screened as soluble phage. The phage ELISA is shown in FIG. 3.

Example 2: Identification of Sequences for Binding dAbs

Binding dAbs were identified as follows. Ninety-six individual colonies (pDOM5) were picked from each of the VH14-15, VH18-19 and VK outputs and expressed in 200 µL Terrific Broth containing OnEx Autoinduction media (Novagen, UK) overnight at 37°C with shaking at 250 rpm in Costar 96 Well Cell Culture Clusters (Corning Incorporated, USA). The cultures were centrifuged to pellet the cells and the supernatants assayed by antigen binding ELISA for CD28 binding dAbs. Maxisorp 96 well immunoplates (Nunc, USA) were coated overnight at 4° C with 1 mg/ml CD28-Fc in PBS then washed. All washes were as described for the phage ELISA. The plates were blocked for 1 hour at room temperature with 200 µl of PBS containing 1% Tween 20 and then washed. The clarified dAb containing culture supernatant was added to the ELISA plate in the presence of either protein A for VH (Sigma, UK) or protein L for VK (Sigma, UK) to increase the ELISA signal strength by cross-linking the VH or VK dAbs respectively. The plates were incubated for 1 hour at room temperature then washed. Bound dAb was detected using a two step process, firstly 9E10 (anti-myc IgG, Sigma-Aldrich, UK) diluted 1:2000 in PBST was added for 1 hour at room temp then washed, followed by anti-mouse Fc-HRP dilute 1:2000 in PBST for 1 hour at room temperature. The plates were washed and the ELISA developed using SureBlue 1-Component TMB MicroWell Peroxidase solution (KPL Inc, USA) and the color allowed to develop. The colorimetric reaction was stopped by the addition of an equal volume of 1 M HCL and the ELISA plate read at 450nm. CD28 specific clones were identified by comparison to a control plate coated with Fc alone (*see* FIG. 4 for example of soluble ELISA). All specific clones were DNA sequenced and initially 28 unique clones were identified (see appendix for sequences). An additional two plates of dAb supernatants were screened for binding to CD28-Fc by BIAcore analysis (GE Healthcare, UK). From this screening, an additional 30 unique sequences were identified.

The dAb amino acid sequences in the examples below do not necessarily correspond exactly to the dAb sequences disclosed in the Sequence Listing. In some cases, the dAb amino acid sequences may contain additional amino acid residues at the N-termninus of the protein, which are introduced to facilitate cloning into an expression vector. In Examples 5, *et seq.*, for instance, the amino acid sequence of recombinatnly expressed dAbs may contain a Ser Thr sequence at the N-terminus. These additional N-terminal residues are not believed to affect the biological activity of the dAbs.

Example 3: Characterization of dAb Binding Properties

To characterize the binding activity of the sequenced dAbs, all 58 clones were expressed and purified and tested on the BIAcore against a CM5 chip coated with 12500 RU (response units) of CD28-Fc. A total of nine clones showed binding, including DOM21-4, DOM21-6, DOM21-18, DOM21-20, DOM21-22, DOM21-27 and DOM21-28 (see FIG. 5 for BIAcore traces) and DOM21-38 and DOM21-44.

The protein concentrations used for BIAcore analysis were as follows:

DOM21-4 42.3 μM

DOM21-6 68.1 μM

DOM21-18 13.8 μM

DOM21-20 57.5 μM

DOM21-22 19.4 μM

DOM21-27 14.7 μM

DOM21-28 16.6 μM.

Several dAbs disclosed and characterized herein have been aligned to compare sequence identity with observed activity;

DOM21-18 (VK) and 1h-239-891 (VK) are 82.4% identical.

DOM21-28 (VK) and 1h-239-891 (VK) are 83.3% identical.

DOM21-28 (VK) and 1h-239-850 (VK) are 85.2% identical.

1h-239-891 (VK) and 1h-239-850 (VK) are 96.3% identical.

DOM21-4 (VH) and 1h-99-238 (VH) are 81.7% identical.

DOM21-20 (VH) and 1h-99-238 (VH) are 78.9% identical.

DOM21-4 (VH) and 1h-239-850 (VK) are 23.9% identical.

```
                      1                                                  50
1h-239-891     (1)    DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYF
  DOM21-18     (1)    DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYQ
                      51                                                 100
1h-239-891     (51)   TSRLRHGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQ
  DOM21-18     (51)   ASLLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQ
                      101
1h-239-891    (101)   GTKVEIKR (SEQ ID NO: 476)
  DOM21-18    (101)   GTKVEIKR (SEQ ID NO: 455)

                      1                                                  50
1h-239-891     (1)    DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYF
  DOM21-28     (1)    DIQMTQSPSSLSASVGDRVTITCRASQSISHSLVWYQQKPGKAPKLLIYW
                      51                                                 100
1h-239-891     (51)   TSRLRHGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQ
  DOM21-28     (51)   ASLLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYTTPFTFGQ
                      101
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1h-239-891  (101) GTKVEIKR (SEQ ID NO: 476)
  DOM21-28  (101) GTKVEIKR (SEQ ID NO: 456)

                    1                                                  50
1h-239-850    (1) DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYF
  DOM21-28    (1) DIQMTQSPSSLSASVGDRVTITCRASQSISHSLVWYQQKPGKAPKLLIYW
                    51                                                 100
1h-239-850   (51) TSRLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQ
  DOM21-28   (51) ASLLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWTTPFTFGQ
                    101
1h-239-850  (101) GTKVEIKR (SEQ ID NO: 58)
  DOM21-28  (101) GTKVEIKR (SEQ ID NO: 456)

                    1                                                  50
1h-239-850    (1) DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYF
1h-239-891    (1) DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYF
                    51                                                 100
1h-239-850   (51) TSRLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQ
1h-239-891   (51) TSRLRHGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQ
                    101
1h-239-850  (101) GTKVEIKR (SEQ ID NO: 58)
1h-239-891  (101) GTKVEIKR (SEQ ID NO: 476)

                  1                                                    50
1h-99-238     (1) EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSW
  DOM21-4     (1) EVQLLESGGGLVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVSV
                  51                                                   100
1h-99-238    (51) IDASGVQTDYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSP
  DOM21-4    (51) IDSLGIQTMYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEYG
                  101             120
1h-99-238   (101) FGPLYCFDYRGQGTLVTVSS (SEQ ID NO: 273)
  DOM21-4   (101) G----AFDYWGQGTLVTVSS (SEQ ID NO: 401)
                  1                                                    50
1h-99-238     (1) EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSW
 DOM21-20     (1) EVQLLESGGGLVQPGGSLRLSCAASGFTFPAYSMIWVRQAPGKGLEWVST
                  51                                                   100
1h-99-238    (51) IEASGVQTDYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSP
 DOM21-20    (51) ISPLGYSTMYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEQT
                  101             123
1h-99-238   (101) FGP---LYGFDYRGQGTLVTVSS (SEQ ID NO: 273)
 DOM21-20   (101) AYLNRATEHFDYWGQGTLVTVSS (SEQ ID NO: 402)

                  1                                                    50
1h-239-850    (1) DIQMTQSPSSLSASVGDRVTITCRASRPIWP--FLEWYQQKPGK-----A
   DOM21-4    (1) EVQLLES-GGGLVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVS
                  51                                                   100
1h-239-850   (44) PKLLIYFTSRLQSGVPSRFSGSGSG--TDFTLTISSLQPEDFATYYCLQN
   DOM21-4   (50) VIDSLGLQTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEY
                  101           117
1h-239-850   (92) VSMPATFSQGTKVEIKR (SEQ ID NO: 58)
   DOM21-4  (100) GGAFDYWGQGTLVTVSS (SEQ ID NO: 401)
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Example 4: *In vitro* dAb Activity Assay

The dAb activity was tested *in vitro* as follows. Seven of the dAbs (DOM21-4, DOM21-6, DOM21-18, DOM21-20, DOM21-22, DOM21-27 and DOM21-28) were expressed and purified on a larger scale. Endotoxin depleted dAbs samples at a stock

concentration of 100 μM were used to determine whether the dAbs could inhibit the activity of CD28 in a cell based *in vitro* assay similar to that described by Boulougouris, *J. Immunol.* 1998, 161(8): 3919-3924. Proliferation assays were performed in triplicate in 96-well plates in a final volume of 200 μl per well using RPMI 1640 medium containing 10% FCS and antibiotics. Human CD4 positive T-cells (5 x 10^4) were cultured in the presence of 1 μg/ml anti-CD3 antibody (OKT3) plus transfected CHO cells expressing either CD80 or CD86 and dAb or control antibody at a range of concentrations. Assays were incubated at 37° C for between 18 hours to 72 hours in the presence of 1 μCi [^{3}H]-thymidine per well. Cells were harvested onto 96-well filter plates using a Packard (Meriden, CT) 96-well harvester, and [^{3}H]-thymidine uptake was determined via liquid scintillation counting. Four dAbs, DOM21-4, DOM21-18, DOM21-20 and DOM21-28 showed inhibitory activity (FIG. 6) with DOM21-4 and DOM21-28 showing the greatest degree of inhibition (FIG. 7).

The DNA sequence of unique dAbs identified in the receptor binding assay as inhibiting CD28 binding to CD80 or CD86 are detailed below. The amino acid sequences are also set forth below, with CDR regions for various dAbs in bold font.

>DOM21-1

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGATGCGTATTCGATGATTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACTATTACTCCGCAGGGTGATAGGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGCAAG
CTGGTTGGAGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:1)

>DOM21-2

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGTGGATTATGAGATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACTATTTCGAATGATGGCGCTGCTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
ATGATGCTGCTTTTGACTACTGGGGTCAGGGAGCCCTGGTCACCGTCTCGAGCG (SEQ
ID NO:2)

>DOM21-3

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTGCGTATTCTATGGGGTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATGGATTACGGGGAATGGTGGTTCTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
CGGAGGAGCCGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:3)

>DOM21-4

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAGTAGGTATCATATGGCGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGTGATTGATTCTCTTGGTCTTCAGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGGAAT
ATGGTGGTGCGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGCG (SEQ
ID NO:4)

>DOM21-5

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTACTCATTATTCTATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACATATTACTCCGGATGGTCTTATTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAG
GTAGGTTGGTTGATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGCG
(SEQ ID NO:5)

>DOM21-6

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGAATTATGGTATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAAATATTGGTCGGGCTGGTAGTGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
TTCAGTCGTGGAGGACTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:6)

>DOM21-7

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTCCTGCGTATTCTATGGGGTGGGTCCGCCAGG
CTCCAGAGAAGGGTCTAGAGTGGGTCTCATATATTGATGGGCGTGGTGCTGAGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGCGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
TTGATACTCTGATTTCTGAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:7)

>DOM21-8

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTCCTAATTATACGATGTGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTAGTGGTACTGGTCATACTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAT
TTGGGCCTAATAATCCTATGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:8)

>DOM21-9

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCGAGTTATGATATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGCGATTTCGGCGGATGGTACGTTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAT
CTTCTTTTGATAAGTATAATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:9)

>DOM21-10

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCTAAGTATACGATGTGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAAGTATTGATCCTGTTGGTAATTTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
GGGGGCCGACGTCGTCTAATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:10)

>DOM21-11

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAGTGAGTATGGTATGAAGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACGATTGATAATGTTGGTTCGGTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
CTACGCCTGTTTTGCTGCCGCTTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:11)

>DOM21-12

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGATTCTTATAATATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTTGAGTGGGTCTCAGCTATTGCGGCTAATGGTCGTGTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
TGACGAATATGGCGTATGGTAGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:12)

>DOM21-13

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGATCTGTATTCGATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCACATATTGATAGGGCTGGTATGATTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
TTTCTAATGCTGTTAATATGCAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:13)

>DOM21-14

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCTAAGTATACGATGTGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAAGTATTGATCCTGTTGGTAATTTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
GTCATAGGCCTTCGACGCAGGATTTTGACTACTGGGGTCAGGGAACCCTGGNCACCGTC
TCGAGC (SEQ ID NO:14)

>DOM21-15

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTCCTGATTATAAGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATGGATTGATAAGGGTGGTATTATTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
TGTTTCCTAAGTTTCGGCCGGCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGCG (SEQ ID NO:15)

>DOM21-16

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGGATTATGGGATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACATATTAATCGTTCTGGTCTGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
TTCTGAATGCTCCTAATTTTAAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGCG (SEQ ID NO:16)

>DOM21-17

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAATCGTTATGCGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATGGATTGATGGTAATGGTCTGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
GGACTAGGTCTCATTCTGATTCGGGTTGGGCTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:17)

>DOM21-18

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACCGTGTCAC
CATCACTTGCCGGGCAAGTCAGTATATTGGTACTTCGTTAAATTGGTACCAGCAGAAAC
CAGGGAAAGCCCCTAAGCTCCTGACCTATCAGGCTTCCTTGTTGCAAAGTGGGGTCCCA
TCACGTTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
ACCTGAAGATTTTGCTACGTACTACTGTCAACAGTTGGCGCTGCGTCCTATGACGTTCG
GCCAAGGGACCAAGGTGGAAATCAAACGGG (SEQ ID NO:18)

>DOM21-19

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTAATTATAATATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGGTATTACGAAGGGTGGTCGGGTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAT
TGGGTCCGTCGAGGATGCTTAATGAGCCGCTGTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGCG (SEQ ID NO:19)

>DOM21-20

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTCCGGCGTATTCGATGATTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACGATTTCGCCGCTGGGTTATTCGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGGAAC
AGACGGCTTATTTGAATCGTGCTACGGAGCATTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGCG (SEQ ID NO:20)

>DOM21-21

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTTCGAAGTATGATATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCATCGATTTATGCTATTGGTGGTAATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAT
TGAAGTCGGGGATGCAGACTCGGTTGAATTCTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGCG (SEQ ID NO:21)

>DOM21-22

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGCTGTATCAGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACTATTATGCCTAGTGGTAATCTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
TGTGGTCGTTGAATTTGGGGTTTCATGCGGCTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:22)

>DOM21-23

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGGCAGTATGGTATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGGGATTAGTCCTTCTGGTAATTATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAG
GGAATGGGTCTCTTCCGCCTCGTGGGTCTATTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGCG (SEQ ID NO:23)

>DOM21-24

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTAATTATAATATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGGTATTACGAAGGGTGGTCGGGTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAT
TGGGTCCGTCGAGGATGCTTAATGAGCCGCTGTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGCG (SEQ ID NO:24)

>DOM21-25

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGGACGTATTATATGGGGTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTGGGGCTAATGGTGCTCCTACATAT
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
TTCGTTCGCTTAATAGGTGGGCGGAGCCTGTGTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:25)

>DOM21-26

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCTGATTATTCTATGTATTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCACAGATTAGTCCGGCGGGTTCTTTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAG
ATTCTAAGTCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGCG (SEQ
ID NO:26)

>DOM21-27

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACCGTGTCAC
CATCACTTGCCGGGCAAGTCAGAGTATTGGGACGGGTTTACGGTGGTACCAGCAGAAAC
CAGGGAAAGCCCCTATGCTCCTGATCTATCGGGCGTCCATTTTGCAAAGTGGGGTCCCA
TCACGTTTTAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
ACCTGAAGATTTTGCTACGTACTACTGTCAACAGACGACTCTTCAGCCTTTTACGTTCA
GCCAAGGGACTAAGGTGGAAATCAAACGGG (SEQ ID NO:27)

>DOM21-28

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACCGTGTCAC
CATCACTTGCCGGGCAAGTCAGTCTATTAGTCATTCGTTAGTTTGGTACCAGCAGAAAC
CAGGGAAAGCCCCTAAGCTCCTGATCTATTGGGCTTCCCTTTTGCAAAGTGGGGTCCCA
TCACGTTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
ACCTGAAGATTTTGCTACGTACTACTGTCAACAGGGTATGACTACGCCTTTTACGTTCG
GCCAAGGGACCAAGGTGGAAATCAAACGGG (SEQ ID NO:28)

>DOM21-30

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGATAGTTATGATATGAATTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCTGCTGATGGTCATTTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAT
CGCGGAGTAGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:29)

>DOM21-31

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAGGGATTATATGATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACGTATTGATTCTCATGGTAATCGTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
ATATGACGGGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:30)

>DOM21-32

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAGGGAGTATATGATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACGTATTAATGGTGTGGGTAATTCTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
ATCAGGTGGGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:31)

>DOM21-33

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAGTGATTATATGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACGTATTACGTCTGAGGGTTCGCATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
ATACGTCTGGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:32)

>DOM21-34

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGGAGGTATATGATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCACGGATTTCTGGTCCTGGTACGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
ATGATACGGGGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:33)

>DOM21-35

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTTCTTCTTATGCTATGATTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGAGATTTCTCCTTATGGTAATCATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
CTGATCGGCGTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:34)

>DOM21-36

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTACTTCGTATGGGATGCAGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCGATTTCTACTGATGGTATGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAC
TTGGGGTTAATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO:35)

>DOM21-37

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTGATTATATGATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCAATTATTCGTGTGCCTGGTTCGACTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
AGAAGGGTGATGAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:36)

>DOM21-38

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTATTCTGTATGATATGCAGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACGTATTTCTGCTAATGGTCATGATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
GTCCGCATTATTTGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:37)

>DOM21-39

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGCGCAGCCTCCGGATTCACCTTTACTAAGTATTTTATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCACTGATTGATCCGCGTGGTCCTCATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
AGTTGGGTGAGGAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:38)

>DOM21-40

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTAAGACTTATACGATGAGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACTATTAATTCGAGTGGTACTTTGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAT
CTAGTTCTTATACGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:39)

>DOM21-41

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCGATGTATAGTATGAAGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCGATTTCGAATGCTGGTGATATTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGGAAT
CGTTTAGGTCTCGTTATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO:40)

>DOM21-42

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGATGATTATCTTATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTGGAGTGGGTCTCACTGATTCGTATGAGGGGTTCTGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
ATTCTCTTACTACTAATCTTTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:41)

>DOM21-43

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTACTGATTATATGATGGCTTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAATTATTGGGACTACTGGTACGTGGACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
CTAATGCGTATGAGAGTGAGTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO:42)

>DOM21-44

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCGCGGTATACTATGGTGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGCTATTCATTTTGATGGTCGGACTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAATAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
ATGAGTGGGCGTCTCTTAAGCATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:43)

>DOM21-45

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGGATTATATGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATTTATTAATCTGCCTGGTGGTCGTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
AGACTCATGGGCTGACTGGTTATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:44)

>DOM21-46

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTTTGTATGGTATGGCTTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCGATTGGGATGCATGGTGATACTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
TTTGTGGGGCTACGTATTGTAATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:45)

>DOM21-47

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTAAGTATGTTATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAATTATTGATTCCTTGGGTTCTACTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
GGGGTTTGTTGGTTCATTATGATTTTGACTACTGGGGTCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO:46)

>DOM21-48

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGGTGTATGGTATGTCTTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATTGATTGATGCGGGTGGTCGGAATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAT
CGACGACGCGTGCTTATAGTGATTATTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC (SEQ ID NO:47)

>DOM21-49

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGAGAATTATGATATGCATTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGGGATTACTACGCATGGTAGGCGTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
GTGATAATTTGAATATGAATGTGGATTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC (SEQ ID NO:48)

>DOM21-50

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTATTAAGTATGATATGTGTTGGGCCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATGTATTGAGTCTAGTGGTCAGAATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAT
GTCTGAATGATAGTTGTAATGTTCATTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC (SEQ ID NO:49)

>DOM21-51

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGTAATTATAATATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAGATATTGGTCGTTATGGTAGGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGATACCGCGGTATATTACTGTGCGAAAA
CTCAGCGTATGGTTAATCCGTCGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC (SEQ ID NO:50)

>DOM21-52

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCTTCCGGATTCACCTTTGTTAGTTATAGTATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAATTATTTCGGGGCAGGGTACTGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAT
CGCCGATGGTTTTTGCTTTGGATGGGAGGTCTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:51)

>DOM21-53

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTACAGCCTCCGGATTCACCTTTTCTGAGTATAGTATGGGGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAAGTATTACGCCTGTTGGTGTTTTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
GGAGGCCTGGGCCGCATGGTTGGTCTTTTCGGTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:52)

>DOM21-54

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGGGCAGTATATGATGGGTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCAACTATTGATAAGTCGGGTTATAGTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAA
GTGGGATTGATTCGCGGGGTCTGATGACTAAGTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:53)

>DOM21-55

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTGCTCGTTATCGTATGGCGTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTCTGAGTGATGGTGCGGTTACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
CTGGGGGGAATGCGTGGTCTACTCGGGTTACTTTTGACTACTGGGGTCAGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:54)

>DOM21-56

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTTTTACGTATACNATGGCTTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTACGCCGCTTGGTTATAATACATAC
TACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAC
CGTCGGATGTGAAGGTGTCTCCGCTGCCGAGTTTTGACTACTGGGGTCGGGGAACCCTG
GTCACCGTCTCGAGC (SEQ ID NO:55)

>DOM21-57

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTCT
CTCCTGTGCAGCCTCCGGATTCACCTTTACTATGTATGGTATGCATTGGGTCCGCCAGG
CTCCAGGGAAGGGTCTAGAGTGGGTCTCATCGATTTCTCAGTATGGTCTTTCTACATAC
TACGCAGATTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACACGCT
GTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGCGAAAG
GGTCTATGAGGCGGGTGTTTAGTAGTTCGGATACTTTTGACTACTGGGGTCAGGGAACC
CTGGTCACCGTCTCGAGC (SEQ ID NO:56)

>DOM21-58

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACCGTGTCAC
CATCACTTGCCGGGCAAGTCAGAATATAGGTGATCGGTTACATTGGTACCAGCAGAAAC
CAGGGAAAGCCCCTAAGCTCCTGATCTATCGTATTTCCCGTTTGCAAAGTGGGGTCCCA
TCACGTTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
ACCTGAAGATTTTGCTACGTACTACTGTCAACAGTTTGGGCTGTATCCTACTACGTTCG
GCCAAGGGACCAAGGTGGAAATCAAACGG (SEQ ID NO:57)

DOM21-4

EVQLLESGGGLVQPGGSLRLSCAASGFTFS**RYHMA**WVRQAPGKGLEWVS**VIDSLGLQTY**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAE**YGGAFDY**WGQGTLVTVSS
(SEQ ID NO:401)

DOM21-20

EVQLLESGGGLVQPGGSLRLSCAASGFTFP**AYSMI**WVRQAPGKGLEWVS**TISPLGYSTY**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAE**QTAYLNRATEHFDY**WGQGTL
VTVSS (SEQ ID NO:402)

DOM21-1

EVQLLESGGGLVQPGGSLRLSCAASGFTFDAYSMIWVRQAPGKGLEWVSTITPQGDRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAQAGWSFDYWGQGTLVTVSS
(SEQ ID NO:403)

DOM21-2

EVQLLESGGGLVQPGGSLRLSCAASGFTFVDYEMAWVRQAPGKGLEWVSTISNDGAATY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDDAAFDYWGQGALVTVSS
(SEQ ID NO:404)

DOM21-3

EVQLLESGGGLVQPGGSLRLSCAASGFTFGAYSMGWARQAPGKGLEWVSWITGNGGSTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKAEEPFDYWGQGTLVTVSS
(SEQ ID NO:405)

DOM21-4

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVSVIDSLGLQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEYGGAFDYWGQGTLVTVSS
(SEQ ID NO:406)

DOM21-5

EVQLLESGGGLVQPGGSLRLSCAASGFTFTHYSMGWVRQAPGKGLEWVSHITPDGLITY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGRLVDFDYWGQGTLVTVSS
(SEQ ID NO:407)

DOM21-6

EVQLLESGGGLVQPGGSLRLSCAASGFTFENYGMAWVRQAPGKGLEWVSNIGRAGSVTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVQSWRTFDYWGQGTLVTVSS
(SEQ ID NO:408)

DOM21-7

EVQLLESGGGLVQPGGSLRLSCAASGFTFPAYSMGWVRQAPEKGLEWVSYIDGRGAETY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKIDTLISEFDYWGQGTLVTVS
S (SEQ ID NO:409)

DOM21-8

EVQLLESGGGLVQPGGSLRLSCAASGFTFPNYTMWWVRQAPGKGLEWVSSISGTGHTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKFGPNNPMFDYWGQGTLVTVS S (SEQ ID NO:410)

DOM21-9

EVQLLESGGGLVQPGGSLRLSCAASGFTFASYDMGWVRQAPGKGLEWVSAISADGTFTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSSFDKYNFDYWGQGTLVTVS S (SEQ ID NO:411)

DOM21-10

EVQLLESGGGLVQPGGSLRLSCAASGFTFAKYTMWWVRQAPGKGLEWVSSIDPVGNLTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRGPTSSNFDYWGQGTLVTVS S (SEQ ID NO:412)

DOM21-11

EVQLLESGGGLVQPGGSLRLSCAASGFTFSEYGMKWVRQAPGKGLEWVSTIDNVGSVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKTTPVLLPLFDYWGQGTLVTV SS (SEQ ID NO:413)

DOM21-12

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSYNMGWVRQAPGKGLEWVSAIAANGRVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMTNMAYGSFDYWGQGTLVTV SS (SEQ ID NO:414)

DOM21-13

EVQLLESGGGLVQPGGSLRLSCAASGFTFDLYSMAWVRQAPGKGLEWVSHIDRAGMITY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVSNAVNMQFDYWGQGTLVTV SS (SEQ ID NO:415)

DOM21-14

EVQLLESGGGLVQPGGSLRLSCAASGFTFAKYTMWWVRQAPGKGLEWVSSIDPVGNLTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRHRPSTQDFDYWGQGTLVTV SS (SEQ ID NO:416)

DOM21-15

EVQLLESGGGLVQPGGSLRLSCAASGFTFPDYKMGWVRQAPGKGLEWVSWIDKGGIITY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMFPKFRPAFDYWGQGTLVTV SS (SEQ ID NO:417)

DOM21-16

EVQLLESGGGLVQPGGSLRLSCAASGFTFEDYGMGWVRQAPGKGLEWVSHINRSGLVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVLNAPNFKFDYWGQGTLVTV SS (SEQ ID NO:418)

DOM21-17

EVQLLESGGGLVQPGGSLRLSCAASGFTFNRYAMGWVRQAPGKGLEWVSWIDGNGLVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRTRSHSDSGWAFDYWGQGTL VTVSS (SEQ ID NO:419)

DOM21-19

EVQLLESGGGLVQPGGSLRLSCAASGFTFGNYNMGWVRQAPGKGLEWVSGITKGGRVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLGPSRMLNEPLFDYWGQGTL VTVSS (SEQ ID NO:420)

DOM21-20

EVQLLESGGGLVQPGGSLRLSCAASGFTFPAYSMIWVRQAPGKGLEWVSTISPLGYSTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEQTAYLNRATEHFDYWGQGTL VTVSS (SEQ ID NO:421)

DOM21-21

EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYDMAWVRQAPGKGLEWVSSIYAIGGNTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLKSGMQTRLNSFDYWGQGTL VTVSS (SEQ ID NO:422)

DOM21-22

EVQLLESGGGLVQPGGSLRLSCAASGFTFELYQMGWVRQAPGKGLEWVSTIMPSGNLTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMWSLNLGFHAAFDYWGQGTL VTVSS (SEQ ID NO:423)

DOM21-23

EVQLLESGGGLVQPGGSLRLSCAASGFTFGQYGMGWVRQAPGKGLEWVSGISPSGNYTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGNGSLPPRGSIFDYWGQGTL VTVSS (SEQ ID NO:424)

DOM21-24

EVQLLESGGGLVQPGGSLRLSCAASGFTFGNYNMGWVRQAPGKGLEWVSGITKGGRVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLGPSRMLNEPLFDYWGQGTL VTVSS (SEQ ID NO:425)

DOM21-25

EVQLLESGGGLVQPGGSLRLSCAASGFTFGTYYMGWARQAPGKGLEWVSSIGANGAPTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKIRSLNRWAEPVFDYWGQGTL VTVSS (SEQ ID NO:426)

DOM21-26

EVQLLESGGGLVQPGGSLRLSCAASGFTFADYSMYWVRQAPGKGLEWVSQISPAGSFTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDSKSFDYWGQGTLVTVSS (SEQ ID NO:427)

DOM21-40

EVQLLESGGGLVQPGGSLRLSCAASGFTFKTYTMRWVRQAPGKGLEWVSTINSSGTLTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSSSYTFDYWGQGTLVTVSS (SEQ ID NO:428)

DOM21-41

EVQLLESGGGLVQPGGSLRLSCAASGFTFAMYSMKWVRQAPGKGLEWVSSISNAGDITY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAESFRSRYFDYWGQGTLVTVSS (SEQ ID NO:429)

DOM21-42

EVQLLESGGGLVQPGGSLRLSCAASGFTFDDYLMGWVRQAPGKGLEWVSLIRMRGSVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHSLTTNLFDYWGQGTLVTVS S (SEQ ID NO:430)

DOM21-43

EVQLLESGGGLVQPGGSLRLSCAASGFTFTDYMMAWARQAPGKGLEWVSIIGTTGTWTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKTNAYESEFDYWGQGTLVTVS S (SEQ ID NO:431)

DOM21-44

EVQLLESGGGLVQPGGSLRLSCAASGFTFARYTMVWVRQAPGKGLEWVSAIHFDGRTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKNEWASLKHFDYWGQGTLVTV SS (SEQ ID NO:432)

DOM21-45

EVQLLESGGGLVQPGGSLRLSCAASGFTFEDYMMGWVRQAPGKGLEWVSFINLPGGRTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQTHGLTGYFDYWGQGTLVTV SS (SEQ ID NO:433)

DOM21-46

EVQLLESGGGLVQPGGSLRLSCAASGFTFGLYGMAWARQAPGKGLEWVSSIGMHGDTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVCGATYCNFDYWGQGTLVTV SS (SEQ ID NO:434)

DOM21-47

EVQLLESGGGLVQPGGSLRLSCAASGFTFGKYVMAWVRQAPGKGLEWVSIIDSLGSTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGGLLVHYDFDYWGQGTLVTV SS (SEQ ID NO:435)

DOM21-48

EVQLLESGGGLVQPGGSLRLSCAASGFTFEVYGMSWARQAPGKGLEWVSLIDAGGRNTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSTTRAYSDYFDYWGQGTLVT VSS (SEQ ID NO:436)

DOM21-49

EVQLLESGGGLVQPGGSLRLSCAASGFTFENYDMHWVRQAPGKGLEWVSGITTHGRRTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSDNLNMNVDFDYWGQGTLVT VSS (SEQ ID NO:437)

DOM21-50

EVQLLESGGGLVQPGGSLRLSCAASGFTFIKYDMCWARQAPGKGLEWVSCIESSGQNTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKCLNDSCNVHFDYWGQGTLVT VSS (SEQ ID NO:438)

DOM21-51

EVQLLESGGGLVQPGGSLRLSCAASGFTFGNYNMGWVRQAPGKGLEWVSDIGRYGRVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKTQRMVNPSPFDYWGQGTLVT VSS (SEQ ID NO:439)

DOM21-52

EVQLLESGGGLVQPGGSLRLSCAASGFTFVSYSMGWVRQAPGKGLEWVSIISGQGTVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPMVFALDGRSFDYWGQGTL VTVSS (SEQ ID NO:440)

DOM21-53

EVQLLESGGGLVQPGGSLRLSCTASGFTFSEYSMGWVRQAPGKGLEWVSSITPVGVFTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGRPGPHGWSFRFDYWGQGTL VTVSS (SEQ ID NO:441)

DOM21-54

EVQLLESGGGLVQPGGSLRLSCAASGFTFGQYMMGWVRQAPGKGLEWVSTIDKSGYSTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSGIDSRGLMTKFDYWGQGTL VTVSS (SEQ ID NO:442)

DOM21-55

EVQLLESGGGLVQPGGSLRLSCAASGFTFARYRMAWVRQAPGKGLEWVSSILSDGAVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPGGNAWSTRVTFDYWGQGTL VTVSS (SEQ ID NO:443)

DOM21-57

EVQLLESGGGLVQPGGSLRLSCAASGFTFTMYGMHWVRQAPGKGLEWVSSISQYGLSTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGSMRRVFSSSDTFDYWGQGT LVTVSS (SEQ ID NO:444)

DOM21-59

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSYDMNWVRQAPGKGLEWVSQISADGHFTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSRSSFDYWGQGTLVTVSS
(SEQ ID NO:445)

DOM21-60

EVQLLESGGGLVQPGGSLRLSCAASGFTFRDYMMGWVRQAPGKGLEWVSRIDSHGNRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHMTGFDYWGQGTLVTVSS
(SEQ ID NO:446)

DOM21-61

EVQLLESGGGLVQPGGSLRLSCAASGFTFREYMMGWVRQAPGKGLEWVSRINGVGNSTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHQVGFDYWGQGTLVTVSS
(SEQ ID NO:447)

DOM21-62

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYMMGWVRQAPGKGLEWVSRITSEGSHTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHTSGFDYWGQGTLVTVSS
(SEQ ID NO:448)

DOM21-63

EVQLLESGGGLVQPGGSLRLSCAASGFTFGRYMMGWVRQAPGKGLEWVSRISGPGTVTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHDTGFDYWGQGTLVTVSS
(SEQ ID NO:449)

DOM21-64

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMIWVRQAPGKGLEWVSEISPYGNHTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPDRRFDYWGQGTLVTVSS
(SEQ ID NO:450)

DOM21-65

EVQLLESGGGLVQPGGSLRLSCAASGFTFTSYGMQWVRQAPGKGLEWVSSISTDGMVTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLGVNFDYWGQGTLVTVSS
(SEQ ID NO:451)

DOM21-66

EVQLLESGGGLVQPGGSLRLSCAASGFTFGDYMMGWVRQAPGKGLEWVSIIRVPGSTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQKGDEFDYWGQGTLVTVSS (SEQ ID NO:452)

DOM21-67

EVQLLESGGGLVQPGGSLRLSCAASGFTFILYDMQWVRQAPGKGLEWVSRISANGHDTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGPHYLFDYWGQGTLVTVSS (SEQ ID NO:453)

DOM21-68

EVQLLESGGGLVQPGGSLRLSCAASGFTFTKYFMGWVRQAPGKGLEWVSLIDPRGPHTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQLGEEFDYWGQGTLVTVSS (SEQ ID NO:454)

DOM21-18

DIQMTQSPSSLSASVGDRVTITC**RASQYIGTSLN**WYQQKPGKAPKLLTY**QASLLQS**GVP SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQLALRPMT**FGQGTKVEIKR (SEQ ID NO:455)

DOM21-28

DIQMTQSPSSLSASVGDRVTITC**RASQSISHSLV**WYQQKPGKAPKLLIY**WASLLQS**GVP SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQGMTTPFT**FGQGTKVEIKR (SEQ ID NO:456)

DOM21-18

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYQASLLQSGVP SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR (SEQ ID NO:457)

DOM21-27

DIQMTQSPSSLSASVGDRVTITCRASQSIGTGLRWYQQKPGKAPMLLIYRASILQSGVP SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTTLQPFTFSQGTKVEIKR (SEQ ID NO:458)

DOM21-28

DIQMTQSPSSLSASVGDRVTITCRASQSISHSLVWYQQKPGKAPKLLIYWASLLQSGVP SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGMTTPFTFGQGTKVEIKR (SEQ ID NO:459)

DOM21-58

DIQMTQSPSSLSASVGDRVTITCRASQNIGDRLHWYQQKPGKAPKLLIYRISRLQSGVP SRFSGSGSGTDFTLTISSLQPEDFATYYCQQFGLYPTTFGQGTKVEIKR (SEQ ID NO:460)

DOM21-30

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSYDMNWVRQAPGKGLEWVSQISADGHFTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSRSSFDYWGQGTLVTVSS (SEQ ID NO:461)

DOM21-31

EVQLLESGGGLVQPGGSLRLSCAASGFTFRDYMMGWVRQAPGKGLEWVSRIDSHGNRTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHMTGFDYWGQGTLVTVSS (SEQ ID NO:462)

DOM21-32

EVQLLESGGGLVQPGGSLRLSCAASGFTFREYMMGWVRQAPGKGLEWVSRINGVGNSTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHQVGFDYWGQGTLVTVSS (SEQ ID NO:463)

DOM21-33

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYMMGWVRQAPGKGLEWVSRITSEGSHTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHTSGFDYWGQGTLVTVSS (SEQ ID NO:464)

DOM21-34

EVQLLESGGGLVQPGGSLRLSCAASGFTFGRYMMGWVRQAPGKGLEWVSRISGPGTVTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKHDTGFDYWGQGTLVTVSS (SEQ ID NO:465)

DOM21-35

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMIWVRQAPGKGLEWVSEISPYGNHTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPDRRFDYWGQGTLVTVSS
(SEQ ID NO:466)

DOM21-36

EVQLLESGGGLVQPGGSLRLSCAASGFTFTSYGMQWVRQAPGKGLEWVSSISTDGMVTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKLGVNFDYWGQGTLVTVSS
(SEQ ID NO:467)

DOM21-37

EVQLLESGGGLVQPGGSLRLSCAASGFTFGDYMMGWVRQAPGKGLEWVSIIRVPGSTTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQKGDEFDYWGQGTLVTVSS
(SEQ ID NO:468)

DOM21-38

EVQLLESGGGLVQPGGSLRLSCAASGFTFILYDMQWVRQAPGKGLEWVSRISANGHDTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGPHYLFDYWGQGTLVTVSS
(SEQ ID NO:469)

DOM21-39

EVQLLESGGGLVQPGGSLRLSCAASGFTFTKYFMGWVRQAPGKGLEWVSLIDPRGPHTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQLGEEFDYWGQGTLVTVSS
(SEQ ID NO:470)

DOM21-56

EVQLLESGGGLVQPGGSLRLSCAASGFTFFTYXMAWVRQAPGKGLEWVSSITPLGYNTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPSDVKVSPLPSFDYWGRGTL
VTVSS (SEQ ID NO:471)

The following additional VH and VK dAbs were prepared, isolated and characterized. The amino acid sequences of various dAbs are set forth below, with CDR1, CDR2, and CDR3 regions for various dAbs in bold font. CDR1, CDR2 and CDR3 amino acid sequences of various dAbs also are separately set forth below.

VK dAbs:

1h-239-850 (SEQ ID NO:58)

DIQMTQSPSSLSASVGDRVTITC**RASRPIWPFLE**WYQQKPGKAPKLLIY**FTSRLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**LQNVSMPAT**FSQGTKVEIKR

1h-35 (SEQ ID NO:59)

DIQMTQSPSSLSASVGDRVTITC**RASQYIGSALS**WYQQKPGKAPKLLIY**RASNLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQLAIRPFT**FGQGTKVEIKR

1h-36 (SEQ ID NO:60)

DIQMTQSPSSLSASVGDRVTITC**RASRDIALDLL**WYQQKPGKAPKLLIK**GWSGLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**AQGWGRPVT**FGQGTKVEIKR

1h-79 (SEQ ID NO:61)

DIQMTQSPSSLSASVGDRVTITC**RASQPIGHSLA**WYQQKPGKAPKLLIY**WASTLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQMLRTPFT**FGQGTKVEIKR

1h-80 (SEQ ID NO:62)

DIQMTQSPSSLSASVGDRVTITC**RASQRIGSNLA**WYQQKPGKAPKLLIY**WASLLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQTRSAPFT**FGQGTKVEIKR

1h-83 (SEQ ID NO:63)

DIQMTQSPSSLSASVGDRVTITC**RASQSIGHSLV**WYQQKPGKAPKLLIY**WASLLQS**GVS
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQSRAAPFT**FGQGTKVEIKR

1h-108 (SEQ ID NO:64)

DIQMTQSPSSLSASVGDRVTITC**RASQYIGTALN**WYQQKPGKAPKLLIY**RRSHLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQIALTPYT**FGQGTKVEIKR

1h-203 (SEQ ID NO:65)

DIQMTQSPSSLSASVGDRVTITC**RASQPIGSVLA**WYQQKPGKAPKLLIY**FSSILQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQALRSPFT**FGQGTKVEIKR

1h-207 (SEQ ID NO:66)

DIQMTQSPSSLSASVGDRVTITC**RASQYIGTSLA**WYQQKPGKAPKLLIY**HSSGLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQTALRPFT**FGQGTKVEIKR

1h-238 (SEQ ID NO:67)

DIQMTQSPSSLSASVGDRVTITC**RASQHINASLG**WYQQKPGKAPKLLIY**WASQLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQMVRTPFT**FGQGTKVEIKR

1h-239 (SEQ ID NO:68)

DIQMTQSPSSLSASVGDRVTITC**RASQSIYPFLE**WYQQKPGKAPKLLIY**FTSRLQS**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**QQNATNPAT**FGQGTKVEIKR

1h-18-1 (SEQ ID NO:69)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYQASFLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR

1h-18-2 (SEQ ID NO:70)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYQASLLQSGVP
SRFSGSGYGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR

1h-18-3 (SEQ ID NO:71)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYRASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR

1h-18-4 (SEQ ID NO:72)

DIQLTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLAYQASLLQSGVP
SRFSGSGYGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR

1h-18-5 (SEQ ID NO:73)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLTYQASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAMRPMTFGQGTKVEIKW

1h-18-6 (SEQ ID NO:74)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLNWYQQKPGKAPKLLIYQASLLQSGVP
SRFSGSGYGTDFTLTISSLQPEDFATYYCQQLALRPMTFGQGTKVEIKR

1h-28-1 (SEQ ID NO:75)

DIQMTQSPSSLSASVGDRVTITCRASQSISHSLVWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGMSTPFTFGQGTKVEIKR

1h-28-2 (SEQ ID NO:76)

DIQMTQSPSSLSASVGDRVTITCRASQSISHSLVWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGMTAPFTFGQGTKVEIKR

1h-31 (SEQ ID NO:77)

DIQMTQSPSSLSASVGDRVTITCRASQSIGYSLAWYQQKPGKAPKLLIYWVSSLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTQRTPFTFGQGTKVEIKR

1h-32 (SEQ ID NO:78)

DIQMTQSPSSLSASVGDRVTITCRASQNIGHGLAWYQQKPGKAPKLLIYWVSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTLSKPFTFGQGTKVEIKR

1h-33 (SEQ ID NO:79)

DIQMTQSPSSLSASVGDRVTITCRASSNIHNRLNWYQQKPGKAPKLLIYAASSLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCRQWIQPPWTFGQGTKVEIKR

1h-34 (SEQ ID NO:80)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLAWYQQKPGKAPKLLIYHSSGLQSGVP
LRFSGSGSGTDFTLTISSLQPEDFATYYCQQTALRPFTFGQGTKVEIKR

1h-35 (SEQ ID NO:81)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALSWYQQKPGKAPKLLIYRASNLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKR

1h-35-15 (SEQ ID NO:82)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALGWYLQKPGKAPKLLIYRASNLQSGVP
SRFSGSGYGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKR

1h-35-2 (SEQ ID NO:83)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALGWYQQKPGKAPKLLIYRASHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKR

1h-35-5 (SEQ ID NO:84)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSAISWYQQKPGRAPKLLIYRASYLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVGIKR

1h-35-7 (SEQ ID NO:85)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALGWYQQKPGKAPKLLIYRASNLQSGVP
SRFSGSGYGTGFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKR

1h-35-9 (SEQ ID NO:86)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALGWYQQKPGKAPKLLIYRASNMQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKR

1h-36 (SEQ ID NO:87)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLLWYQQKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGWGRPVTFGQGTKVEIKR

1h-36-1 (SEQ ID NO:88)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDILWYQQKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCARGWGRPVTFGQGTKVEIKR

1h-36-2 (SEQ ID NO:89)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDILWYQQKPGKAPKLLIKGWSGLQSEVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAKGWGRPVTFGQGTKVEIKR

1h-36-3 (SEQ ID NO:90)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLMWYQQKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGWGRPVTFGQGTKVEIKR

1h-36-4 (SEQ ID NO:91)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLSWYQHKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTINSLQPEDFATYYCAQGWGRPVTFGQGTKVEIKR

1h-36-5 (SEQ ID NO:92)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLSWYQQKPGRAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGWGRPETFGQGTKVEIKR

1h-36-6 (SEQ ID NO:93)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLLWYQLKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYFCAQGWGRPVTFGQGTKVEIKR

1h-36-7 (SEQ ID NO:94)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLLWYQQKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGWGRPATFGQGTKVEIKR

1h-38 (SEQ ID NO:95)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISGLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-39 (SEQ ID NO:96)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALHWYQQKPGKAPRLLIYLSSNLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSALNPYTFGQGTKVEIKR

1h-69 (SEQ ID NO:97)

DIQMTQSPSSLSASVGDRVTITCRASQKIGTGLRWYQQKPGKAPKLLIYRASVLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTAFPPYTFGQGTKVEIKR

1h-70 (SEQ ID NO:98)

DIQMTQSPSSLSASVGDRVTITCRASQSIGTGLRWYQQKPGKAPMLLIYRASILQSGVP
SRFSGGGSGTDFTLTISSLQPEDFATYYCQQTWYRPYTFGQGTKVEIKR

1h-71 (SEQ ID NO:99)

DIQMTQSPSSLSASVGDRVTITCRASRDIGHMLNWYQQKPGKAPKLLIWFGSVLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCVQGRLRPPTFGQGTKVEIKR

1h-72 (SEQ ID NO:100)

DIQMTQSPSSLSASVGDRVTITCRASRSINHWLDWYQQKPGKAPTLLISGVSWLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCCQPGFRPCTFGQGTKVEIKR

1h-73 (SEQ ID NO:101)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTQLSWYQQKPGKAPKLLIYRGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTALSPYTFGQGTKVEIKR

1h-74 (SEQ ID NO:102)

DIQMTQSPSSLSASVGDRVTITCRASQYIGGALSWYQQKPGKAPKLLIYRASRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQVALVPYTFGQGTKVEIKR

1h-75 (SEQ ID NO:103)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTRLSWYQQKPGKAPKLLIYNASFLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLALSPLTFGQGTKVEIKR

1h-76 (SEQ ID NO:104)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTRLVWYQQKPGKAPKLLIYQSSLLQSGVP
SRFRGSGSGTDFTLTISSLQPEDSATYYCQQTALVPYTFGQGTKVEIKR

1h-77 (SEQ ID NO:105)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPRLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSASMPITFGQGTKVEIKR

1h-78 (SEQ ID NO:106)

DIQMTQSPSSLSASVGDRVTITCRASQNIGHMLAWYQQKPGKAPKLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQARAAPFTFGQGTKVEIKR

1h-79 (SEQ ID NO:107)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-1 (SEQ ID NO:108)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFGWYQQKPGKAPKLLIYWASTLQSGVP
TRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-10 (SEQ ID NO:109)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLFYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-11 (SEQ ID NO:110)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQMLRTPFTFGHGTKVEIKR

1h-79-15 (SEQ ID NO:111)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTITISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-1505 (SEQ ID NO:112)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWGSWLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-1512 (SEQ ID NO:113)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASVLLHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-1519 (SEQ ID NO:114)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASLLLDGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-1520 (SEQ ID NO:115)

DIQMTQSPSSLSASVGDRVAITCRASQPIGHSLGWYEQKPGKAPKLLIYWSSVLISGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-16 (SEQ ID NO:116)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYFCQQMLRTPFTFGQGTKVEIKR

1h-79-17 (SEQ ID NO:117)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFAFGQGTKVEIKR

1h-79-18 (SEQ ID NO:118)

DIQMTQSSSSLSASVGDRVSITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPADSATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-19 (SEQ ID NO:119)

DIQMTQSPSSRSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-2 (SEQ ID NO:120)

DTQMTQSPSSLSASVGDRVTITCRASRPIGHSLGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-20 (SEQ ID NO:121)

DIQMTQSPSSLSASVGDRVTVTCRASQPIGHSLAWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-21 (SEQ ID NO:122)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-22 (SEQ ID NO:123)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLAWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFSFGQGTKVEIKR

1h-79-23 (SEQ ID NO:124)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-24 (SEQ ID NO:125)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFAFGQGTKVEIKR

1h-79-25 (SEQ ID NO:126)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFAFGQGTKVEIKR

1h-79-26 (SEQ ID NO:127)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFSFGQGTKVEIKR

1h-79-27 (SEQ ID NO:128)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFSFGQGTKVEIKR

1h-79-28 (SEQ ID NO:129)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-29 (SEQ ID NO:130)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFAFGQGTKVEIKR

1h-79-3 (SEQ ID NO:131)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLRPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-30 (SEQ ID NO:132)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFSFGQGTKVEIKR

1h-79-31 (SEQ ID NO:133)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-32 (SEQ ID NO:134)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFAFGQGTKVEIKR

1h-79-4 (SEQ ID NO:135)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPRLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-5 (SEQ ID NO:136)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVENKR

1h-79-6 (SEQ ID NO:137)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSFAWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQREDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-7 (SEQ ID NO:138)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLTYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFTFGQGTKVEIKR

1h-79-8 (SEQ ID NO:139)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-801 (SEQ ID NO:140)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWGSDLYKGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-802 (SEQ ID NO:141)

DIQMTQSPSSLSASVGDRVTITCRASTPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-803 (SEQ ID NO:142)

DIQMTQSPSSLSASVGDRVTITCRASQSIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-804 (SEQ ID NO:143)

DIQMTQSPSSLSASVGDRVTITCRASKPISHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-805 (SEQ ID NO:144)

DIQMTQSPSSLSASVGDRVTITCRASQAIDHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-806 (SEQ ID NO:145)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASMLQGGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-807 (SEQ ID NO:146)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHTLGWYQQKPGKAPKLLIYWASDLIRGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-808 (SEQ ID NO:147)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHALGWYQQKPGKAPRLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-809 (SEQ ID NO:148)

DIQMTQSPSSLSASVGDRVTITCRASQAIGHSLGWYQQKPGKAPKLLVYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-810 (SEQ ID NO:149)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWGSDLSYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-811 (SEQ ID NO:150)

DIQMTQSPSSLSASVGDRVTITCRASRSIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-812 (SEQ ID NO:151)

DIQMTQSPSSLSASVGDRVTITCRASSTIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-813 (SEQ ID NO:152)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMMRTPFMFGQGTKVEIKR

1h-79-814 (SEQ ID NO:153)

DIQMTQSPSSLSASVGDRVTITCRASSRIGSSLGWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-815 (SEQ ID NO:154)

DIQMTQSPSSLSASVGDRVTITCRASRAIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMLRTPFMFGQGTKVEIKR

1h-79-9 (SEQ ID NO:155)

DIQMTQSPSSLSASVGDRVTITCRASQPIGHSLGWYQQKPGKAPKLLIYWASTLQSGVP
SRFSGSGSGTDFTLTISSLQPADFATYYCQQMLRTPFTFGRGTKVEIKR

1h-80 (SEQ ID NO:156)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-1 (SEQ ID NO:157)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGRAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLIISSLQPEDFATYYCQQTRSAPFAFGQGTKVEIKR

1h-80-10 (SEQ ID NO:158)

DLQMTQSPSSLSASVGDSVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-11 (SEQ ID NO:159)

DFQMTQSPSSLSASVGDRVTITCRAGQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-12 (SEQ ID NO:160)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLVYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-2 (SEQ ID NO:161)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSETDFTLTISSLQPEDFATYYCQQTRSAPFAFGQGTKVEIKR

1h-80-3 (SEQ ID NO:162)

DIQMTQSPSSLSESIGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQNGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-4 (SEQ ID NO:163)

DIQMIQSPSSLSASVGERVTIICQASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGSDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-5 (SEQ ID NO:164)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTINSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-6 (SEQ ID NO:165)

DIQMTQSPSSLSASVGDRVTITCRASQGIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQETRSAPFTFGQGTKVEIKR

1h-80-7 (SEQ ID NO:166)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGSDFTLTISSLQPEDFATYYCQETRSAPFTFGQGTKVEIKR

1h-80-8 (SEQ ID NO:167)

DLQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDYATYYCQQTRSAPFTFGQGTKVEIKR

1h-80-9 (SEQ ID NO:168)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSATDFTLTISSLRPEDFATYYCQQTRSAPFAFGQGTKVEIKR

1h-81 (SEQ ID NO:169)

DIQMTQSPSSLSASVGDRVTITCRASQEIDHGLAWYQQKPGKAPKLLIYWASRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQVVAAPFTFGQGTKVEIKR

1h-82 (SEQ ID NO:170)

DIQMTQSPSSLSASVGDRVTITCRASQDIGLNLLWYQQKPGKAPTLLIYWSSMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGRMRPFTFGQGTKVEIKR

1h-83 (SEQ ID NO:171)

DIQMTQSPSSLSASVGDRVTITCRASQSIGHSLVWYQQKPGKAPKLLIYWASLLQSGVS
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSRAAPFTFGQGTKVEIKR

1h-84 (SEQ ID NO:172)

DIQMTQSPSSLSASVGDRVTITCRASQSIGKGLMWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSLRTPFTFGQGTEVEIKR

1h-85 (SEQ ID NO:173)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKAPRLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQSLRTPFTFGQGTKVEIKR

1h-86 (SEQ ID NO:174)

DIQMTQSPSSLSASVGDRVTITCRASQDIGQSLVWYQQKPGKAPKLLIYWASMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQVMRRPFTFGQGTKVEIKR

1h-87 (SEQ ID NO:175)

DIQMTQSPSSLSASVGDRVTITCRASQSIGKSLAWYQQKPGKAPKLLIYWVSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIVSRPFTFGQGTKVEIKR

1h-88 (SEQ ID NO:176)

DIQMTQSPSSLSASVGDRVTITCRASQAISNGLLWYQQKPGKAPKLLIYWTSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQVLRRPFTFGQGTKVEIKR

1h-89 (SEQ ID NO:177)

DIQMTQSPSSLSASVGDRVTITCRASQDIANSLVWYQQKPGKAPKLLIYWVSILQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTIAAPFTFGQGTKVEIKR

1h-90 (SEQ ID NO:178)

DIQMTQSPSSLSASVGDRVTITCRASQTIGHGLVWYQQKPGKAPKLLIYWSSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTLRTPFTFGQGTKVEIKR

1h-107 (SEQ ID NO:179)

DIQMTQSPSSLSASVGDRVTITCRASQYIGNALAWYQQKPGKAPKLLIYRGSYLQSGVP
SRFSGSGSRTDFTLTISSLQPEDFATYYCQQTALRPLTFGQGTKVEIKR

1h-108 (SEQ ID NO:180)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPKLLIYRRSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-108-1 (SEQ ID NO:181)

DIQMTQSPSTLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-108-10 (SEQ ID NO:182)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-108-11 (SEQ ID NO:183)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPKLLIYRGSHLLSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQIALTPYTFGQGTKVEIKR

1h-108-12 (SEQ ID NO:184)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGEAPKLLIYRRSHLQSGVP
SRFSGSGSETDFTLTISSLQPEDFVTYYCQQIALTPYTFGQGTKVEIKR

1h-108-2 (SEQ ID NO:185)

DIQMTQSPSSLSASVGDRVTISCRASQYIGTALNWYQQKPGEAPKLLIYRRSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPFTFGQGTKVEIKR

1h-108-3 (SEQ ID NO:186)

DIQMTQSPTSLSASVGDRVIITCRASQYIGTALNWYQQKPGKAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-108-4 (SEQ ID NO:187)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKRGKAPELLIYRRSHLQSGVP
SRFSGSGYGTDFTLTISSLQPEDFATYYCQQIALTPYTFSQGTKVEIKR

1h-108-5 (SEQ ID NO:188)

DIQITQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPELLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFVTYYCQQIALTPYTFGQGTKVEIKR

1h-108-6 (SEQ ID NO:189)

DIQITQSPSSLSASVGDRVTFTCQASQYIGTALNWYQQKPGKAPKLLIYRGSHLQGGVP
SRFSGSGSGTDFTLTISSLQLEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-108-7 (SEQ ID NO:190)

DIQMTQSPSSLSASVGDRVTITCQASQYIGTALNWYQQKPGKAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIER

1h-108-8 (SEQ ID NO:191)

DIQMTQSPSSLSASVGDRVIITCRASQYIGTALNWYQQKPGNAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISSLLPEDYATYYCQQIALTPYTFSQGTKVEIKR

1h-108-9 (SEQ ID NO:192)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKAPKLLIYRGSHLQSGVP
SRFSGSGSGTDFTLTISGLQPEDFATFYCQQIALTPYTFGQGTKVEIKR

1h-109 (SEQ ID NO:193)

DIQMTQSPSSLSASVGDRVTITCRASQDIGASLLWYQQKPGKAPKLLIYFSSMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSGMRPFTFGQGTKVEIKR

1h-110 (SEQ ID NO:194)

DIQMTQSPSSLSASVGDRVTITCRASRDIGHMLNWYQQKPGKAPKLLIWFGSVLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCVQGRLRPPTFGQGTKVEIKR

1h-111 (SEQ ID NO:195)

DIQMTQSPSSLSASVGDRVTITCRASRSIGHQLVWYQQKPGKAPKLLIAWSSVLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCRQDLSLPFTFGQGTKVEIKR

1h-116 (SEQ ID NO:196)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPRLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNATNPATFGQGTKVEIKR

1h-200 (SEQ ID NO:197)

DIQMTQSPSSLSASVGDRVTITCRASRDIALDLLWYQQKPGKAPKLLIKGWSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGWGRPVTFGQGTKVEIKC

1h-201 (SEQ ID NO:198)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISGLQPEDFATYYCQQALRSPFTFGQGTKVEIKC

1h-202 (SEQ ID NO:199)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKAPRLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQSLRTPFTFGQGTKVEIKC

1h-203 (SEQ ID NO:200)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-203-1 (SEQ ID NO:201)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVIAWYQQKPGKAPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-203-2 (SEQ ID NO:202)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQRGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-203-3 (SEQ ID NO:203)

DILMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQRGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-204 (SEQ ID NO:204)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTRLVWYQQKPGKAPKLLIYQSSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDSATYYCQQTALVPYTFGQGTKVEIKR

1h-205 (SEQ ID NO:205)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKAPRLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSLRTPFTFGQGTKVEIKR

1h-207 (SEQ ID NO:206)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLAWYQQKPGKAPKLLIYHSSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTALRPFTFGQGTKVEIKR

1h-208 (SEQ ID NO:207)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALHWYQQKPGKAPKLLIYLSSNLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSALNPYTFGQGTKVEIKR

1h-209 (SEQ ID NO:208)

DIQMTQSPSSLSASVGDRVTITCRASQDIGLNLLWYQQKPGKAPKLLIYWSSMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGRMRPFTFGQGTKVEIKR

1h-217 (SEQ ID NO:209)

DIQMTQSPSSLSASVGDRVTITCRASQSIGYSLAWYQQKPGKAPKLLIYWVSSLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTQRTPFTFGQGTKVEIKC

1h-218 (SEQ ID NO:210)

DIQMTQSPSSLSASVGDRVTITCRASQYIGSALSWYQQKPGKAPKLLIYRASNLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQLAIRPFTFGQGTKVEIKC

1h-219 (SEQ ID NO:211)

DIQMTQSPSSLSASVGDRVTITCRASQYIGGALSWYQQKPGKAPKLLIYRASRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQVALVPYTFGQGTKVEIKC

1h-220 (SEQ ID NO:212)

DIQMTQSPSSLSASVGDRVTITCRASQRIGSNLAWYQQKPGKAPKLLIYWASLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTRSAPFTFGQGTKVEIKC

1h-221 (SEQ ID NO:213)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKAPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQALRSPFTFGQGTKVEIKC

1h-223 (SEQ ID NO:214)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKAPRLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQSLRTPFTFGQGTKVEIKC

1h-225 (SEQ ID NO:215)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTSLAWYQQKPGKAPKLLIYHSSGLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTALRPFTFGQGTKVEIKC

1h-227 (SEQ ID NO:216)

DIQMTQSPSSLSASVGDRVTITCRASQDIGLNLLWYQQKPGKAPKLLIYWSSMLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQGRMRPFTFGQGTKVEIKC

1h-228 (SEQ ID NO:217)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKAPKLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQSLRTPFTFGQGTKVEIKC

1h-229 (SEQ ID NO:218)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTRLVWYQQKPGKAPKLLIYQSSLLQSGVP
SRFRGSGSGTDFTLTISSLQPEDFATYYCQQTALVPYTFGQGTKVEIKC

1h-231 (SEQ ID NO:219)

DIQMTQSPSSLSASVGDRVTITCRASQSIGYSLAWYQQKPGKDPKLLIYWVSSLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTQRTPFTFGQGTKVEIKR

1h-232 (SEQ ID NO:220)

DIQMTQSPSSLSASVGDRVTITCRASQPIGSVLAWYQQKPGKDPKLLIYFSSILQSGVP
SRFSGSGSGTDFTLTISGLQPEDFATYYCQQALRSPFTFGQGTKVEIKR

1h-233 (SEQ ID NO:221)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTRLVWYQQKPGKDPKLLIYQSSLLQSGVP
SRFRGSGSGTDFTLTISSLQPEDSATYYCQQTALVPYTFGQGTKVEIKR

1h-234 (SEQ ID NO:222)

DIQMTQSPSSLSASVGDRVTITCRASQPIGASLLWYQQKPGKDPKLLIYWGSLLQSGVP
SRFSGSGSGTDFTLTISSLQPEDLATYYCQQSLRTPFTFGQGTKVEIKR

1h-235 (SEQ ID NO:223)

DIQMTQSPSSLSASVGDRVTITCRASQTIGHGLVWYQQKPGKDPKLLIYWSSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQTLRTPFTFGQGTKVEIKR

1h-236 (SEQ ID NO:224)

DIQMTQSPSSLSASVGDRVTITCRASQYIGTALNWYQQKPGKDPKLLIYRRSHLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQIALTPYTFGQGTKVEIKR

1h-237 (SEQ ID NO:225)

DIQMTQSPSSLSASVGDRVTITCRASQHINASLGWYQQKPGKDPKLLIYWASQLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMVRTPFTFGQGTKVEIKR

1h-238 (SEQ ID NO:226)

DIQMTQSPSSLSASVGDRVTITCRASQHINASLGWYQQKPGKAPKLLIYWASQLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMVRTPFTFGQGTKVEIKR

1h-239 (SEQ ID NO:227)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNATNPATFGQGTKVEIKR

1h-239-8 (SEQ ID NO:228)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-804 (SEQ ID NO:229)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-807 (SEQ ID NO:230)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-809 (SEQ ID NO:231)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-815 (SEQ ID NO:232)

DIQMTQSPSSLSASVGDRVTITCRASQPIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-816 (SEQ ID NO:233)

DIQMTQSPSSLSASVGDRVTITCRASRTIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-817 (SEQ ID NO:234)

DIQMTQSPSSLSASVGDRVTITCRASKPIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-819 (SEQ ID NO:235)

DIQMTQSPSSLSASVGDRVTITCRASQAIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-824 (SEQ ID NO:236)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLRQGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-828 (SEQ ID NO:237)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLREGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-829 (SEQ ID NO:238)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFSSRLASGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-832 (SEQ ID NO:239)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSYLREGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-833 (SEQ ID NO:240)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-837 (SEQ ID NO:241)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLASGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-838 (SEQ ID NO:242)

DIQMTQSPSSLSASVGDRVTITCQASQSIYPFLEWYQQKPGKAPKLLIYFTSRLARGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTRVEIKR

1h-239-840 (SEQ ID NO:243)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFASRLASGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-847 (SEQ ID NO:244)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLAYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIRR

1h-239-849 (SEQ ID NO:245)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSKLTRGVP
SRFSGSGSGADFTLTISNLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-850 (SEQ ID NO:246)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-851 (SEQ ID NO:247)

DIQMTQSPSSLSASVGDRVTITCRASRNIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-856 (SEQ ID NO:248)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-857 (SEQ ID NO:249)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPAAFSQGTKVEIKR

1h-239-859 (SEQ ID NO:250)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFSSMLASGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-861 (SEQ ID NO:251)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNVSMPATFSQGTKVEIKR

1h-239-862 (SEQ ID NO:252)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLAYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNVSMPATFSQGTKVEIKR

1h-239-863 (SEQ ID NO:253)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRQGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNVSMPATFSQGTKVEIKR

1h-239-864 (SEQ ID NO:254)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQNVSMPATFSQGTKVEIKR

1h-239-869 (SEQ ID NO:255)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-870 (SEQ ID NO:256)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVMMPATFSQGTKVEIKR

1h-239-871 (SEQ ID NO:257)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-872 (SEQ ID NO:258)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-873 (SEQ ID NO:259)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLAYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-874 (SEQ ID NO:260)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRQGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-875 (SEQ ID NO:261)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-876 (SEQ ID NO:262)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-877 (SEQ ID NO:263)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-879 (SEQ ID NO:264)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTKVEIKR

1h-239-880 (SEQ ID NO:265)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPAAFSQGTKVEIKR

1h-239-881 (SEQ ID NO:266)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLARGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFSQGTRVEIKR

1h-239-882 (SEQ ID NO:267)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-883 (SEQ ID NO:268)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVSMPATFSQGTKVEIKR

1h-239-885 (SEQ ID NO:269)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-886 (SEQ ID NO:270)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-887 (SEQ ID NO:472)

IQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVPS
RFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-888 (SEQ ID NO:473)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLAYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-889 (SEQ ID NO:474)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRQGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-890 (SEQ ID NO:475)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLARGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891 (SEQ ID NO:476)

DIQMTQSPSSLSASVGDRVTITC**RASRPIWPFLE**WYQQKPGKAPKLLIY**FTSRLRH**GVP
SRFSGSGSGTDFTLTISSLQPEDFATYYC**LQNVANPAT**FSQGTKVEIKR

1h-239-892 (SEQ ID NO:477)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-893 (SEQ ID NO:478)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-894 (SEQ ID NO:479)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLAYGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-895 (SEQ ID NO:480)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLRQGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-896 (SEQ ID NO:481)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLARGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-897 (SEQ ID NO:482)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-898 (SEQ ID NO:483)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVQMPATFSQGTKVEIKR

1h-239-9 (SEQ ID NO:271)

DIQMTQSPSSLSASVGDRVTITCRASQSIYPFLEWYQQKPGKAPKLLIYFTSRLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVTNPATFGQGTKVEIKR

1h-112 (SEQ ID NO:397)

DIQMTQSPSSLSASVGDRVTITCRASQHINASLGWYQQKPGKAPRLLIYWASQLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCQQMVRTPFTFGQGTKVEIKR

1h-239-89101 (SEQ ID NO:532)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89102 (SEQ ID NO:533)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89103 (SEQ ID NO:534)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFTQGTKVEIKR

1h-239-89104 (SEQ ID NO:535)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-891(Q3C) (SEQ ID NO:536)

DICMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(S9C) (SEQ ID NO:537)

DIQMTQSPCSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(R18C) (SEQ ID NO:538)

DIQMTQSPSSLSASVGDCVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(G41C) (SEQ ID NO:539)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPCKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(K42C) (SEQ ID NO:540)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGCAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(K45C) (SEQ ID NO:541)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPCLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(S60C) (SEQ ID NO:542)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
CRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(D70C) (SEQ ID NO:543)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTCFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(T74C) (SEQ ID NO:544)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLCISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(Q79C) (SEQ ID NO:545)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLCPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-891(K103C) (SEQ ID NO:546)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLRHGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTCVEIKR

1h-239-89201 (SEQ ID NO:547)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89202 (SEQ ID NO:548)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFFQGTKVEIKR

1h-239-89203 (SEQ ID NO:549)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFQQGTKVEIKR

1h-239-89204 (SEQ ID NO:550)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFVQGTKVEIKR

1h-239-89205 (SEQ ID NO:551)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89206 (SEQ ID NO:552)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFIQGTKVEIKR

1h-239-89207 (SEQ ID NO:553)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFTQGTKVEIKR

1h-239-89208 (SEQ ID NO:554)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFMQGTKVEIKR

1h-239-89209 (SEQ ID NO:555)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFDQGTKVEIKR

1h-239-89210 (SEQ ID NO:556)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFYQGTKVEIKR

1h-239-89211 (SEQ ID NO:557)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNLANPATFSQGTKVEIKR

1h-239-89212 (SEQ ID NO:558)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNTANPATFSQGTKVEIKR

1h-239-89213 (SEQ ID NO:559)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNAANPATFSQGTKVEIKR

1h-239-89214 (SEQ ID NO:560)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCIQNVANPATFSQGTKVEIKR

1h-239-89215 (SEQ ID NO:561)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCHQNVANPATFSQGTKVEIKR

1h-239-89216 (SEQ ID NO:562)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCFQNVANPATFSQGTKVEIKR

1h-239-89217 (SEQ ID NO:563)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCMQNVANPATFSQGTKVEIKR

1h-239-89227 (SEQ ID NO:564)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSYLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89228 (SEQ ID NO:565)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSQLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89229 (SEQ ID NO:566)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSELAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89230 (SEQ ID NO:567)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSILAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89231 (SEQ ID NO:568)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSTLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89232 (SEQ ID NO:569)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSSLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89233 (SEQ ID NO:570)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSDLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89234 (SEQ ID NO:571)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSMLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89218 (SEQ ID NO:572)

DIQMTQSPSSLSASVGDRVTITCRASRWIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89219 (SEQ ID NO:573)

DIQMTQSPSSLSASVGDRVTITCRASRRIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89220 (SEQ ID NO:574)

DIQMTQSPSSLSASVGDRVTITCRASREIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89221 (SEQ ID NO:575)

DIQMTQSPSSLSASVGDRVTITCRASRTIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89222 (SEQ ID NO:576)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89223 (SEQ ID NO:577)

DIQMTQSPSSLSASVGDRVTITCRASRAIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89224 (SEQ ID NO:578)

DIQMTQSPSSLSASVGDRVTITCRASRDIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89225 (SEQ ID NO:579)

DIQMTQSPSSLSASVGDRVTITCRASRFIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89226 (SEQ ID NO:580)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89235 (SEQ ID NO:581)

DIQMTQSPSSLSASVGDRVTITCRASRKIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89236 (SEQ ID NO:582)

DIQMTQSPSSLSASVGDRVTITCRASRYIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFSQGTKVEIKR

1h-239-89237 (SEQ ID NO:583)

DIQMTQSPSSLSASVGDRVTITCRASRPIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNIANPATFSQGTKVEIKR

1h-239-89238 (SEQ ID NO:584)

DIQMTQSPSSLSASVGDRVTITCRGSRTIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89239 (SEQ ID NO:585)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSTLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFTQGTKVEIKR

1h-239-89240 (SEQ ID NO:586)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFTQGTKVEIKR

1h-239-89241 (SEQ ID NO:587)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89242 (SEQ ID NO:588)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89243 (SEQ ID NO:589)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89244 (SEQ ID NO:590)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89245 (SEQ ID NO:591)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSTLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89246 (SEQ ID NO:592)

DIQMTQSPSSLSASVGDRVTITCRASRTIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFAQGTKVEIKR

1h-239-89247 (SEQ ID NO:593)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89248 (SEQ ID NO:594)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSRLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFTQGTKVEIKR

1h-239-89249 (SEQ ID NO:595)

DIQMTQSPSSLSASVGDRVTITCRASRNIWPFLEWYQQKPGKAPKLLIYFTSTLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-89250 (SEQ ID NO:596)

DIQMTQSPSSLSASVGDRVTITCRASRSIWPFLEWYQQKPGKAPKLLIYFTSTLAAGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQNVANPATFPQGTKVEIKR

1h-239-850 CDR1 (SEQ ID NO:484)

RASRPIWPFLE

1h-239-850 CDR2 (SEQ ID NO:485)

FTSRLQS

1h-239-850 CDR3 (SEQ ID NO:486)

LQNVSMPAT

1h-35 CDR1 (SEQ ID NO:487)

RASQYIGSALS

1h-35 CDR2 (SEQ ID NO:488)

RASNLQS

1h-35 CDR3 (SEQ ID NO:489)

QQLAIRPFT

1h-36 CDR1 (SEQ ID NO:490)

RASRDIALDLL

1h-36 CDR2 (SEQ ID NO:491)

GWSGLQS

1h-36 CDR3 (SEQ ID NO:492)

AQGWGRPVTFGQGTKVEIKR

1h-79 CDR1 (SEQ ID NO:493)

RASQPIGHSLA

1h-79 CDR2 (SEQ ID NO:494)

WASTLQS

1h-79 CDR3 (SEQ ID NO:495)

QQMLRTPFT

1h-80 CDR1 (SEQ ID NO:496)

RASQRIGSNLA

1h-80 CDR2 (SEQ ID NO:497)

WASLLQS

1h-80 CDR3 (SEQ ID NO:498)

QQTRSAPFT

1h-83 CDR1 (SEQ ID NO:499)

RASQSIGHSLV

1h-83 CDR2 (SEQ ID NO:500)

WASLLQS

1h-83 CDR3 (SEQ ID NO:501)

QQSRAAPFTFGQGTKVEIKR

1h-108 CDR1 (SEQ ID NO:502)

RASQYIGTALN

1h-108 CDR2 (SEQ ID NO:503)

RRSHLQS

1h-108 CDR3 (SEQ ID NO:504)

QQIALTPYT

1h-203 CDR1 (SEQ ID NO:505)

RASQPIGSVLA

1h-203 CDR2 (SEQ ID NO:506)

FSSILQS

1h-203 CDR3 (SEQ ID NO:507)

QQALRSPFT

1h-207 CDR1 (SEQ ID NO:508)

RASQYIGTSLA

1h-207 CDR2 (SEQ ID NO:509)

HSSGLQS

1h-207 CDR3 (SEQ ID NO:510)

QQTALRPFT

1h-238 CDR1 (SEQ ID NO:511)

RASQHINASLG

1h-238 CDR2 (SEQ ID NO:512)

WASQLQS

1h-238 CDR3 (SEQ ID NO:513)

QQMVRTPFT

1h-239 CDR1 (SEQ ID NO:514)

RASQSIYPFLE

1h-239 CDR2 (SEQ ID NO:515)

FTSRLQS

1h-239 CDR3 (SEQ ID NO:516)

QQNATNPAT

1h-239-891 CDR1 (SEQ ID NO:636)

RASRPIWPFLE

1h-239-891 CDR2 (SEQ ID NO:637)

FTSRLRH

1h-239-891 CDR3 (SEQ ID NO:638)

LQNVANPAT

VH dAbs:

1h-99-237 (SEQ ID NO:272)

EVQLLESGGGLVQPGGSLRLSCAASGFTFD**SANMS**WARQAPGKGLEWVS**WIEAPGVQTF**
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR**SPFGPLYGFDY**RGQGTLVTV
SS

1h-99-238 (SEQ ID NO:273)

EVQLLESGGGLVQPGGSLRLSCAASGFTFD**SANMS**WARQAPGKGLEWVS**WIEASGVQTF**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK**SPFGPLYGFDY**RGQGTLVTV
SS

1h-37 (SEQ ID NO:274)

EVQLLESGGGLVQPGGSLRLSCAASGFTFG**TYKMV**WVRQAPGKGLEWVS**SIGPGGLDTY**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK**SWMTLPITGFDY**RGQGTLVT
VSS

1h-93 (SEQ ID NO:275)

EVQLLESGGGLVQPGGSLRLSCAASGFTFP**LYEMA**WVRQAPGKGLEWVS**SIMSNGIRTY**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK**RKSSSSRTVFDY**WGQGTLVT
VSS

1h-99 (SEQ ID NO:276)

EVQLLESGGGLVQPGGSLRLSCAASGFTFD**SANMT**WVRQAPGKGLEWVS**WIDDTGTQTY**
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK**SPFGPLYGFDY**WGQGTLVTV
SS

1h-4-1 (SEQ ID NO:277)

EVQLLESGGGWVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVSVIDSLGLQAY
YADSVKGRFTISRDNSKNTLYLQMNSMRAEDTAVYYCAEYSGAFDYWGQGTLVTVSS

1h-4-2 (SEQ ID NO:278)

EVQLLESGGGLVQPGGSLHLSCAASGFTFTRYHMAWVRQAPGKGLEWVSVIDSLGLQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEYGGAFDYWGQGTLVTVSS

1h-4-3 (SEQ ID NO:279)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVSVIDSLGLQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEYSGAFDYWGQGTLVTVSS

1h-4-4 (SEQ ID NO:280)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRYHMAWVRQAPGKGLEWVSVIDSLGLQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAEYGGAFDYWGPGTLVTVSS

1h-29 (SEQ ID NO:281)

EVQLLESGGGLVQPGGSLRLSCAASGFTFEDYDMNWVRQAPGKGLEWVSHIDRGGTLTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSTLMGFDYWGQGTLVTVSS

1h-30 (SEQ ID NO:282)

EVQLLESGGGLVQPGGSLRLSCAASGFTFAHYHMGWVRQAPGKGLEWVSWIPADGLRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKYEGAFDYWGQGTLVTVSS

1h-37 (SEQ ID NO:283)

EVQLLESGGGLVQPGGSLRLSCAASGFTFGTYKMVWVRQAPGKGLEWVSSIGPGGLDTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSWMTLPITGFDYRGQGTLVT
VSS

1h-40 (SEQ ID NO:284)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKTYTMRWVRQAPGKGLEWVSTINSSGTLTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSSSYTFDYWGQGTLVTVSS

1h-91 (SEQ ID NO:285)

EVQLLESGGGLVQPGGSLRLSCAASGFTFWFYDMQWVRQAPGKGLEWVSSITHNGKTTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDGQLTFDYWGQGTLVTVSS

1h-92 (SEQ ID NO:286)

EVQLLESGGGLVQPGGSLRLSCAASGFTFELYQMGWVRQAPGKGLEWVSTIMPSGNLTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKMWSLNLGFHAAFDYWGQGTL
VTVSS

1h-93 (SEQ ID NO:287)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPLYEMAWVRQAPGKGLEWVSSIMSNGIRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRKSSSSRTVFDYWGQGTLVT
VSS

1h-93-1 (SEQ ID NO:288)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPLYEMAWVRQAPGKGLEWVSSIMSNGTRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRESSSSRTVFDYWGQGTLVT
VSS

1h-93-2 (SEQ ID NO:289)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPLYEMAWVRQAPGKGLEWVSSIMSNGIRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKRESSSSRTVFDYWGQGTLVT
VSS

1h-93-201 (SEQ ID NO:290)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSVSEMAWVRQAPGKGLEWVSSIMSNGIRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARRESSSSRTVFDYWGQGTLVT
VSS

1h-93-204 (SEQ ID NO:291)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYTAEMAWVRQAPGKGLEWVSSIMSNGIRTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARRESSSSRTVFDYWGQGTLVT
VSS

1h-94 (SEQ ID NO:292)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPGYTMEWVRQAPGKGLEWVSSITPLGANTY
YADSVKGRFTISRDNSRNTLYLQMNSLRAEDTAVYYCAKDIRYTGTYNFDYWGQGTLVT
VSS

1h-95 (SEQ ID NO:293)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPTYAMGWVRQAPGKGLEWVSFIPGAGGVTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKAVDGLANAFDYWGQGTLVTV
SS

1h-96 (SEQ ID NO:294)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMIWVRQAPGKGLEWVSEISPYGNHTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPDRRFDYWGQGTLVTVSS

1h-97 (SEQ ID NO:295)

EVQLLESGGGLVQPGGSLRLSCAASGFTFHSYHMTWVRQAPGKGLEWVSWIDAHGFTTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSRGGPLSTFDYWGQGTLVTV
SS

1h-98 (SEQ ID NO:296)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDTETMHWVRQAPGKGLEWVSSIYVPGSYTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGRHSDVEFDYWGQGTLVTVS
S

1h-99 (SEQ ID NO:297)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKGLEWVSWIDDTGTQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYWGQGTLVTV
SS

1h-99-1 (SEQ ID NO:298)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKGLEWVSWIEDTGTQTF
YADSVRGRFTISRDNFKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2 (SEQ ID NO:299)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-201 (SEQ ID NO:300)

EVQLLESGGGLVQPGGSLRLSCAASGFTFHRWNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-202 (SEQ ID NO:301)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRHNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-203 (SEQ ID NO:302)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYKANMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-204 (SEQ ID NO:303)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVRQNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-205 (SEQ ID NO:304)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMSSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-206 (SEQ ID NO:305)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPLHNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-207 (SEQ ID NO:306)

EVQLLESGGGLVQPGGSLRLSCAASGFTFRASNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-208 (SEQ ID NO:307)

EVQLLESGGGLVQPGGSLRLSCAASGFTFESSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-209 (SEQ ID NO:308)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDKANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-210 (SEQ ID NO:309)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYTSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-211 (SEQ ID NO:310)

EVQLLESGGGLVQPGGSLRLSCAASGFTFASANMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2112 (SEQ ID NO:311)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2113 (SEQ ID NO:312)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWARQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2114 (SEQ ID NO:313)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWARQAPGKGLEWVSWIEAIGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2115 (SEQ ID NO:314)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWVRQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-2116 (SEQ ID NO:315)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWVRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-212 (SEQ ID NO:316)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-213 (SEQ ID NO:317)

EVQLLESGGGLVQPGGSLRLSCAASGFTFQHSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-214 (SEQ ID NO:640)

EVQLLESGGGLVQPGGSLRLSCAASGFTFMRANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-215 (SEQ ID NO:318)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDEANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-216 (SEQ ID NO:319)

EVQLLESGGGLVQPGGSLRLSCAASGFTFTRANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-217 (SEQ ID NO:320)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRSNMSWGRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-218 (SEQ ID NO:321)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDKSNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-219 (SEQ ID NO:322)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKLSNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-220 (SEQ ID NO:323)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYRSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-221 (SEQ ID NO:324)

EVQLLESGGGLVQPGGSLRLSCAASGFTFARSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-222 (SEQ ID NO:325)

EVQLLESGGGLVQPGGSLRLSCAASGFTFQRSNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-223 (SEQ ID NO:326)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSYANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-224 (SEQ ID NO:327)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSHNNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-225 (SEQ ID NO:328)

EVQLLESGGGLVQPGGSLRLSCAASGFTFRLQNMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-226 (SEQ ID NO:329)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKSANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-227 (SEQ ID NO:330)

EVQLLESGGGLVQPGGSLRLSCAASGFTFNHANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNYKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-228 (SEQ ID NO:331)

EVQLLESGGGLVQPGGSLRLSCAASGFTFHRANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGSDYRGQGTLVTV
SS

1h-99-229 (SEQ ID NO:332)

EVQLLESGGGLVQPGGSLRLSCAASGFTFARTNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-230 (SEQ ID NO:333)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIESIGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-231 (SEQ ID NO:334)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEASGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-232 (SEQ ID NO:335)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEALGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDSRGQGTLVTV
SS

1h-99-233 (SEQ ID NO:336)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEASGRQTF
YADSVKGRFTISRDNSKNTLYLQMNGLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-234 (SEQ ID NO:337)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEAAGPQTF
YADSVKGRFTISRDNSKDTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-235 (SEQ ID NO:338)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIENGGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-236 (SEQ ID NO:339)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEAPGKQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGRGTLVTV
SS

1h-99-237 (SEQ ID NO:340)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-238 (SEQ ID NO:341)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-241 (SEQ ID NO:342)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIENNGPQTF
YADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-243 (SEQ ID NO:343)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWGRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-244 (SEQ ID NO:344)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIESSGPQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-245 (SEQ ID NO:345)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEASGFQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-246 (SEQ ID NO:346)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEASGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-247 (SEQ ID NO:347)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEDQGVQTF
YADSVKGRFTISRDNSKSTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-248 (SEQ ID NO:348)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEDIGIQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-249 (SEQ ID NO:349)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEDIGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-250 (SEQ ID NO:350)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEATGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-251 (SEQ ID NO:351)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAEGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-252 (SEQ ID NO:352)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIESSGYQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-253 (SEQ ID NO:353)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKDLEWVSWIEDSGIQTF
YADSVKGRFTISRDNSRNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-254 (SEQ ID NO:354)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIESSGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-255 (SEQ ID NO:355)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIESRGPQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-256 (SEQ ID NO:356)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEAIGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-257 (SEQ ID NO:357)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEDGGLQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-258 (SEQ ID NO:358)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIESHGGQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-259 (SEQ ID NO:359)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEGSGQQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-260 (SEQ ID NO:360)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEANGPQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-261 (SEQ ID NO:361)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-263 (SEQ ID NO:362)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYKANMSWVRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-264 (SEQ ID NO:363)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDKSNMSWVRQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-265 (SEQ ID NO:364)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDKSNMSWARQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-266 (SEQ ID NO:365)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYRSNMSWVRQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-267 (SEQ ID NO:366)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYRSNMSWVRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-268 (SEQ ID NO:367)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKSANMSWVRQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-269 (SEQ ID NO:368)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKSANMSWVRQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-270 (SEQ ID NO:369)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYKANMSWARQAPGKGLEWVSWIEASGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-275 (SEQ ID NO:370)

EVQLLESGGGLVQPGGSLRLSCAASGFTFKDKNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-276 (SEQ ID NO:371)

EVQLLESGGGLVQPGGSLRLSCAASGFTFNRANMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-277 (SEQ ID NO:372)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAVGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-278 (SEQ ID NO:373)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPHSNMSWARQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-297 (SEQ ID NO:374)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAIGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-6 (SEQ ID NO:375)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKGLEWVSWIDDTGTQTF
YEDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-11 (SEQ ID NO:376)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKGLEWVSWIDDIGSQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-13 (SEQ ID NO:377)

EVQLWESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKDLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYRGQGTLVTV
SS

1h-99-14 (SEQ ID NO:378)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWVRQAPGKGLEWVSWIEDTGTQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYWGQGTLVTV
SS

1h-99-15 (SEQ ID NO:379)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMTWVRQAPGKGLEWVSWIDDIGSQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYWGQGTLVTV
SS

1h-100 (SEQ ID NO:380)

EVQLLESGGGLVQPGGSLRLSCAASGFTFESYWMSWVRQAPGKGLEWVSTIADTGGLTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVAYVLDDQPAFDYWGQGTLV
TVSS

1h-101 (SEQ ID NO:381)

EVQLLESGGGLVQPGGSLRLSCAASGFTFGDVSMGWVRQAPGKGLEWVSGIDGPGSNTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKNHAGSTRNVFDYWSQGTLVT
VSS

1h-102 (SEQ ID NO:382)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYSMSWVRQAPGKGLEWVSSIRPSGLSTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKQRARRYQDRPRFDYWGQGTL
VTVSS

1h-103 (SEQ ID NO:383)

EVQLLESGGGLVQPGGSLRLSCAAAGFTFDHTEMGWVRQAPGKGLEWVSAITSDGLNTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGQDRPPWSFDYWGQGTLVTV
SS

1h-104 (SEQ ID NO:384)

EVQLLESGGGLVQPGGSLRLSCADSGLTFSSYAMSWVRQAPGKGLEWVSSISTDGMGTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKYLSAPVLMAYDYWGQGTLVT
VSS

1h-105 (SEQ ID NO:385)

EVQLLESGGGLVQPGGSLRLSCAASGFTFPPYTMGWVRQAPGKGLEWVSWISSSGRKTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKFRKSSVLRSMFDYWGQGTLV
TVSS

1h-106 (SEQ ID NO:386)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSRYPMSWVRQAPGKGLEWVSTIGGLGKTTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAESNMYRSIKYPFAYWGQGTLV TVSS

1h-113 (SEQ ID NO:387)

EVQLLESGGGLVQPGGSLRLSCAASGFTFAKYGMGWVRQAPGKGLEWVSGINGSGIWTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGHVHSPPRGPFLFDYWGQGT LVTVSS

1h-114 (SEQ ID NO:388)

EVQLLESGGGLVQPGGSLRLSCAASGFTFASYSMAWVRQAPGKGLEWVSTIMPSGQRTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKNQSHQRRGIFDYWGQGTLVT VSS

1h-115 (SEQ ID NO:389)

EVQLLESGGGLVQPGGSLRLSCAASGFTFSEYSMAWVRQAPGKGLEWVSHISRDGEFTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGNADLGWVQPHLFVYWGQGT LVTVSS

1h-117 (SEQ ID NO:390)

EVQLLESGGGLVQPGGSLRLSCAASGFTFWRYNMGWARQAPGKGLEWVSSISPTGSITY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKWIGLMSLHPADFDYWGQGTL VTVSS

1h-118 (SEQ ID NO:391)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDTETMHWVRQAPGKGLEWVSSIYVPGSYTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGRHSDVEFDYWGQGTLVTVS S

1h-119 (SEQ ID NO:392)

EVQLLESGGGLVQPGGSLRLSCAASGFTFTDRCMMWVRQAPGKGLEWVSSIQVEGNHTY YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKCMTVGPGNSFDYWGQGTLVT VSS

1h-212 (SEQ ID NO:393)

EVQLLESGGGLVQPGGSLRLSCAASGFTFGTYKMVWVRQAPGKGLEWVSSIGPGGLDTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSWMTLPITGFDYWGQGTLVT
VSS

1h-212-1 (SEQ ID NO:394)

EVQLLESGGGLVQPGGSLRLSCAASGITFGTYKMVWVRQAPGKGLEWVSSIGPGGLDTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAISWMTLPITGFDYWGQGTLVT
VSS

1h-213 (SEQ ID NO:395)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSAAMTWVRQAPGKGLEWVSWIDDTGTQTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSPFGPLYGFDYWGQGTLVTV
SS

1h-230 (SEQ ID NO:396)

EVQLLESGGGLVQPGGSLRLSCAASGFTFGTYKMVWVRQAPGKGLEWVSSIGPGGLDTY
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKSWMTLPITGFDYWGQGTLVT
VSC

1h-99-262 (SEQ ID NO:398)

EVQLLESGGGLVQPGGSLRLSCAASGFTFYKANMSWVRQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23701 (SEQ ID NO:597)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTY
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23702 (SEQ ID NO:598)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVSGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23703 (SEQ ID NO:599)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVQGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23704 (SEQ ID NO:600)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23705 (SEQ ID NO:601)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVHGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23706 (SEQ ID NO:602)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVFGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23707 (SEQ ID NO:603)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVLGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23708 (SEQ ID NO:604)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVPGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYRGQGTLVTV
SS

1h-99-23709 (SEQ ID NO:605)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPAGPLYGFDYRGQGTLVTV
SS

1h-99-23710 (SEQ ID NO:606)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPWGPLYGFDYRGQGTLVTV
SS

1h-99-23711 (SEQ ID NO:607)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPEGPLYGFDYRGQGTLVTV
SS

1h-99-23712 (SEQ ID NO:608)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPSGPLYGFDYRGQGTLVTV
SS

1h-99-23713 (SEQ ID NO:609)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPGGPLYGFDYRGQGTLVTV
SS

1h-99-23714 (SEQ ID NO:610)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPKGPLYGFDYRGQGTLVTV
SS

1h-99-23715 (SEQ ID NO:611)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGTLYGFDYRGQGTLVTV
SS

1h-99-23716 (SEQ ID NO:612)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGALYGFDYRGQGTLVTV
SS

1h-99-23717 (SEQ ID NO:613)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGELYGFDYRGQGTLVTV
SS

1h-99-23718 (SEQ ID NO:614)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGRLYGFDYRGQGTLVTV
SS

1h-99-23719 (SEQ ID NO:615)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGFLYGFDYRGQGTLVTV
SS

1h-99-23720 (SEQ ID NO:616)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYTGQGTLVTV
SS

1h-99-23721 (SEQ ID NO:617)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYVGQGTLVTV
SS

1h-99-23722 (SEQ ID NO:618)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYLGQGTLVTV
SS

1h-99-23723 (SEQ ID NO:619)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYWGQGTLVTV
SS

1h-99-23724 (SEQ ID NO:620)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYFGQGTLVTV
SS

1h-99-23725 (SEQ ID NO:621)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYSGQGTLVTV
SS

1h-99-23726 (SEQ ID NO:622)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYMGQGTLVTV
SS

1h-99-23727 (SEQ ID NO:623)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYKGQGTLVTV
SS

1h-99-23728 (SEQ ID NO:624)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYHGQGTLVTV
SS

1h-99-23729 (SEQ ID NO:625)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYIGQGTLVTV
SS

1h-99-23730 (SEQ ID NO:626)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPLGPLYGFDYRGQGTLVTV
SS

1h-99-23731 (SEQ ID NO:627)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPRGPLYGFDYRGQGTLVTV
SS

1h-99-23732 (SEQ ID NO:628)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYYGQGTLVTV
SS

1h-99-23733 (SEQ ID NO:629)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGPLYGFDYQGQGTLVTV
SS

1h-99-23734 (SEQ ID NO:630)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPRGPLYGFDYRGQGTLVTV
SS

1h-99-23735 (SEQ ID NO:631)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPMGILYGFDYRGQGTLVTV
SS

1h-99-23736 (SEQ ID NO:632)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPHGPLYGFDYRGQGTLVTV
SS

1h-99-23738 (SEQ ID NO:633)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF
YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPMGPLYGFDYRGQGTLVTV
SS

1h-99-23739 (SEQ ID NO:634)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPFGALYGFDYRGQGTLVTV SS

1h-99-23737 (SEQ ID NO:635)

EVQLLESGGGLVQPGGSLRLSCAASGFTFDSANMSWARQAPGKGLEWVSWIEAPGVQTF YADSVRGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPKGPLYGFDYRGQGTLVTV SS

1h-99-237 CDR1 (SEQ ID NO:517)

SANMS

1h-99-237 CDR2 (SEQ ID NO:518)

WIEAPGVQTFYADSVRG

1h-99-237 CDR3 (SEQ ID NO:519)

SPFGPLYGFDY

1h-99-238 CDR1 (SEQ ID NO:520)

SANMS

1h-99-238 CDR2 (SEQ ID NO:521)

WIEASGVQTFYADSVKG

1h-99-238 CDR3 (SEQ ID NO:522)

SPFGPLYGFDY

1h-37 CDR1 (SEQ ID NO:523)

TYKMV

1h-37 CDR2 (SEQ ID NO:524)

SIGPGGLDTYYADSVKG

1h-37 CDR3 (SEQ ID NO:525)

SWMTLPITGFDY

1h-93 CDR1 (SEQ ID NO:526)

LYEMA

1h-93 CDR2 (SEQ ID NO:527)

SIMSNGIRTYYADSVKG

1h-93 CDR3 (SEQ ID NO:528)

RKSSSSRTVFDY

1h-99 CDR1 (SEQ ID NO:529)

SANMT

1h-99 CDR2 (SEQ ID NO:530)

WIDDTGTQTYYADSVKG

1h-99 CDR3 (SEQ ID NO:531)

SPFGPLYGFDY

Example 5: Additional Assays for dAb Activity

The following additional biological assays were used to examine the effect of the dAbs on CD28 activity.

Mixed Lymphocyte Response Cytokine Assays

For MLR experiments measuring cytokines at various time points in response to MoDCs as stimulator cells, assays were performed by combining 1.5 x 10^5 T cells/well of a 96-well round-bottom plate with 1.5 x 10^4 allogeneic MoDCs in a total volume of 300 µL of 10% FCS-RPMI. Titrations of CD28 domain antibodies, abatacept or belatacept were added in triplicate to measure cytokine release at 24, 48, and 72 hours after initiation of the MLR. IL-2 and TNF-α were detected in supernatants using Duoset ELISA development kits (R&D Systems; Minneapolis, MN). IFNγ was measured using paired antibodies and recombinant cytokine from Pierce Biotechnology (Rockford, IL). All kits and Abs were used according to the manufacturer's recommendations. Assay plates were processed and read on a SpectraMax Plus spectrophotometer (Molecular Devices Corp., Sunnyvale, CA). Data was analyzed using Softmax software by comparison against a standard curve generated using recombinant cytokines at known concentrations.

IL-2 Reporter Assay ("Luciferase assay")

Jurkat-CA cells, transfected with the luciferase gene under the control of the IL-2 promoter were cultured in RPMI 1640 (Life Technologies, Inc. Gaithersburg, MD), with 10% FCS (Summit Bio- technology, Ft. Collins., CO.), 1% 1-glutamine, 1% sodium pyruvate, 25 mM HEPES and 0.4 mg/ml Geneticin (all from Life Technologies, Inc.). Raji cells (ATCC, Rockville, MD) were cultured in RPMI 1640, with 10% FCS, 1% 1-glutamine. To initiate Jurkat cell activation, both Jurkat-CA cells and Raji cells were plated at 1.0 x 10^6 cells/ml each in a 96-well opaque plate (Perkin Elmer, Boston, MA). The combined cells are incubated with anti CD3 clone UCHT1 (0.1 μg/ml; BD Pharmingen, San Diego, CA) and dAbs at varying concentrations. After 16-20 hours, the plates were cooled to room temperature and Steady-Glo™ (Promega, Madison, WI) added to the plates. The plates were analyzed using a Topcount-NXT instrument (Perkin Elmer) within 30 minutes of addition of Steady-Glo.

Mixed Lymphocyte Reaction (MLR) Assays

PBMC were obtained by density-gradient separation (Lymphocyte Separation Media; Mediatech Inc., Herndon, VA) of EDTA-treated whole blood from normal healthy donors. T cells were prepared from E^+ fractions of PBMC rosetted with SRBC (Colorado Serum Company; Denver, CO). Mature MoDC were prepared by adherence of monocytes from E fractions of PBMC from normal donors in 6-well tissue culture plates, followed by extensive gentle washing to remove non-adherent cells. Adherent cells were cultured for 7 days in RPMI containing either 10% FCS together with 100 ng/ml GM-CSF and 50 ng/ml IL-4, with one-half the medium changed every other day and replaced with fresh medium containing the same concentration of cytokines. On day 7, cells were matured with LPS (1 μg/ml) for 24 hours. These matured MoDC were then used as antigen-presenting cells in mixed lymphocyte reactions (MLR).

For MLR proliferation assays measuring titrations of CD28 domain antibodies, T cells were cultured at 1 x 10^5 cells/well in triplicate wells together with 2 x 10^3 of allogeneic MoDC as APC in 96-well round-bottom plates in a total volume of 200 μl of 10% FCS-RPMI. Domain antibodies were added at range of concentrations from 100 μg/ml to 10 ng/ml, dependent on relative potency. On day 5 after initiation of the MLR, cultures were pulsed with one μCi of ^{3}[H]-thymidine (PerkinElmer, Boston, MA) for 6 hours, harvested on

a Packard cell harvester (PerkinElmer), and subjected to liquid scintillation counting using a Packard TopCount-NXT instrument (PerkinElmer).

FIG. 3 illustrates the inhibition of T cell proliferation *in vivo* using dAb 1m74-15-P40L. On day "-1", 30 x 10^6 cells/ml splenocytes obtained from DO11 T cell receptor mice were injected into BALB/c mice via the tail vein. On day zero, mice were intraperitoneally dosed with PBS, dAb or CTLA-4 Ig. Two hours after this intraperitoneal dosing, mice were injected in the footpad with 50 mg chicken ovalbumin emulsified 1:1 with Complete Freund's Adjuvant. On days one and two, were dosed intraperitoneally. On day three, draining popliteal lymph nodes were collected for staining with anti-CD4 APC and clonotypic antibody KJ-126 PE (FIG. 3). In FIG. 3, CD4 and KJ126 double positive cells represent antigen-specific T cells. Blood was collected from the animals for exposure, in order to determine the levels of dAb in the blood.

FIGS. 4A and 4B illustrate the results of a nine-day receptor occupancy (RO) study using dAb 1m74-15-P40L. Naïve BALB/c mice were injected intraperitoneally (FIG. 4A) or subcutaneously (FIG. 4B) with either PBS or 1m74-15 40L at 1-, 3-, or 10 mg/kg (n=4). Blood was collected from the animals at time points of 1, 4, 24, 48, 72, 96, 168, and 216 hours. For the dAb treated groups, 50 µl blood was used for staining with anti-CD4 APC and anti-CD28 PE and 50 µl blood was used for exposure. For the PBS groups, 50 µl blood was used for staining with anti-CD4 APC and anti-CD28 PE, and 50 µl blood was used for staining with anti-CD4 and anti-CD28 PE in the presence of excessive non-labeled anti-CD28 antibody to define non-specific binding. Mean fluorescence intensity (MFI) was used as a unit of measure of antibody binding. Percent receptor occupancy (%RO) was defined as "1- [CD28MFI(dAb) – CD28 MFI (non-specific)] / [CD28MFI(PBS) – CD28 MFI (non-specific)]".

Co-Agonist Assays

PBMC were obtained by density-gradient separation (Lymphocyte Separation Media; Mediatech Inc., Herndon, VA) of EDTA-treated whole blood from normal healthy donors. T cells were prepared from E^+ fractions of PBMC rosetted with SRBC (Colorado Serum Company; Denver, CO). T cells were cultured at 1 X 10^5 cells/well in a total volume of 200 µl of 10% FCS-RPMI in triplicate wells of 96-well flat-bottom plates which had been previously coated with 20 µg/ml of anti-CD3 antibody (G19-4 mAb, Bristol-Myers Squibb)

and washed prior to the assay. Domain antibodies were added at range of concentrations from 100 μg/ml to 0.3 μg/ml. Anti-CD28 (9.3 mAb, Bristol-Myers Squibb; Gibson et al. (1996) *Am Soc. Biochem. Mol. Bio.*, 271:7079-7083), 1.0 μg/ml, was used as a positive control. On day 3 after initiation of the assay, cultures were pulsed with one μCi of ^{3}[H]-thymidine (PerkinElmer, Boston, MA) for 6 h, harvested on a Packard cell harvester (PerkinElmer), and subjected to liquid scintillation counting in a Packard TopCount NXT instrument (PerkinElmer).

FIG. 2 illustrates that anti-human CD28 dAbs set forth herein do not exhibit co-agonist activity. Purified T cells (1 X 10^5 cells/well) were added to 96-well flat-bottom plates coated with anti-CD3 (G19-4, 10 μg/ml in PBS). Each dAb, at a final concentration of 30 μg/ml, was added to cells in triplicate wells. As a positive control, anti-CD28 mAb (9.3) was added at a final concentration of 1 μg/ml in place of the dAb. Proliferation was measured by ^{3}[H]-thymidine incorporation on day 3 (FIG. 2).

Agonist Assays

PBMC were obtained by density-gradient separation (Lymphocyte Separation Media; Mediatech Inc., Hemdon, VA) of EDTA-treated whole blood from normal healthy donors. PBMC were cultured at t X 10^5 cells/well in a total volume of 200 μl of 10% FCS-RPMI in triplicate wells of 96-well flat-bottom plates. The dAbs were added in a range of concentrations from 100 μg/ml to 0.3 μg/ml. Anti-CD3 (OKT3), 1 μg/ml in solution, was used as a positive control for maximal proliferation. Anti-CD28 (9.3, 10 μg/ml in solution), together with goat anti-mouse IgG (Jackson Immunoresearch, used at 50 μg/ml in solution) was also used as a comparator in some assays. On day 3 after initiation of the assay, cultures were pulsed with one μCi of 3[H]-thymidine (PerkinElmer, Boston, MA) for 6 hours, harvested on a Packard cell harvester (PerkinElmer), and subjected to liquid scintillation counting using a Packard TopCount NXT instrument (PerkinElmer).

FIGS. 1A and 1B illustrate that anti-human CD28 dAbs set forth herein do not exhibit agonist activity. In a first experiment, PBMC were isolated from whole blood of normal donors and seeded into 96-well flat-bottom plates at 1 X 10^5 cells/well. Several dAbs as set forth herein were added to triplicate wells at the final concentrations indicated FIG. 1A. Anti-CD3 (OKT3, 1 μg/ml final concentration), was included as a positive control. Proliferation was measured by ^{3}[H]-thymidine incorporation on day 3

(FIG. 1A). In a separate experiment, several dAbs set forth herein, anti-CD28 antibody (9.3), anti-CD3 antibody (OKT3), or isotype control were added to triplicate wells in a 96-well round-bottom plate at the final concentrations indicated and allowed to air-dry onto the wells. PBMC were added (1 X 10^5 cells/well) and proliferation was measured by ^{3}[H]-thymidine incorporation on day 3.

The data obtained for dAbs in both the IL-2 reporter assay and in the mixed-lymphocyte reaction assay is assembled for comparison in Table 1 below. Based on the results of these experiments, as well as the results of the co-agonist experiments described herein, it is shown that the dAbs set forth herein bind with affinity and specificity to CD28, and that the dAbs are antagonistic with respect to CD28 activity. The dAbs also demonstrate little to no CD28 agonistic activity.

Table 1: Results of MLR assays and luciferase assays using dAbs set forth herein.

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
VK dAbs:		
1h-239-850 (SEQ ID NO:58)	9 ± 6 nM	2 ± 1 nM
1h-35 (SEQ ID NO:59)	1.9 ± 0.5 μM	2 ± 0.5 μM
1h-36 (SEQ ID NO:60)	570 ± 220 nM	1.8 ± 1 μM
1h-79 (SEQ ID NO:61)	3.8 ± 0.6 μM	3.2 ± 0.5 μM
1h-80 (SEQ ID NO:62)	685 ± 370 nM	2 ± 0.4 μM
1h-83 (SEQ ID NO:63)	1.3 ± 0.5 μM	1.7 ± 1 μM
1h-108 (SEQ ID NO:64)	1.9 ± 0 μM	2.7 ± 0.9 μM
1h-203 (SEQ ID NO:65)	880 ± 140 nM	-----
1h-207 (SEQ ID NO:66)	2.6 μM	-----
1h-238 (SEQ ID NO:67)	775 ± 260 nM	-----

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-239 (SEQ ID NO:68)	1.3 ± 0.1 μM	-----
1h-18-1 (SEQ ID NO:69)	5.4 ± 0.3 μM	-----
1h-18-3 (SEQ ID NO:71)	1 ± 0 μM	-----
1h-18-5 (SEQ ID NO:73)	>7 μM	-----
1h-18-6 (SEQ ID NO:74)	1.4 ± 0.1 μM	-----
1h-31 (SEQ ID NO:77)	800 ± 140 nM	-----
1h-32 (SEQ ID NO:78)	4.5 μM	-----
1h-33 (SEQ ID NO:79)	1.6 ± 0.1 μM	-----
1h-34 (SEQ ID NO:80)	2.9 ± 0.4 μM	-----
1h-35 (SEQ ID NO:81)	1.9 ± 0.5 μM	2 ± 0.5 μM
1h-35-2 (SEQ ID NO:83)	279 ± 93 nM	197 ± 72 nM
1h-35-5 (SEQ ID NO:84)	261 ± 30 nM	248 ± 16 nM
1h-35-7 (SEQ ID NO:85)	79 ± 9 nM	270 ± 102 nM
1h-35-9 (SEQ ID NO:86)	278 ± 11 nM	318 ± 11 nM
1h-36 (SEQ ID NO:87)	570 ± 220 nM	1.8 ± 1 μM
1h-36-6 (SEQ ID NO:93)	162 ± 86 nM	260 ± 120 nM
1h-38 (SEQ ID NO:95)	650 ± 70 nM	725 ± 204 nM
1h-39 (SEQ ID NO:96)	1.3 ± 0.5 μM	-----

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-69 (SEQ ID NO:97)	>7 μM	-----
1h-70 (SEQ ID NO:98)	6.6 μM	-----
1h-71 (SEQ ID NO:99)	3.5 ± 0.7.μM	-----
1h-72 (SEQ ID NO:100)	3.4 ± 1 μM	-----
1h-73 (SEQ ID NO:101)	4.9 ± 1 μM	-----
1h-74 (SEQ ID NO:102)	1.3 ± 0.3 μM	-----
1h-75 (SEQ ID NO:103)	5.7 ± 1 μM	-----
1h-76 (SEQ ID NO:104)	1.8 ± 0.3 μM	-----
1h-79 (SEQ ID NO:107)	3.8 ± 0.6 μM	3.2 ± 0.5 μM
1h-79-1 (SEQ ID NO:108)	418 ± 90 μM	2.1 ± 1.5 μM
1h-79-15 (SEQ ID NO:111)	40 nM	268 ± 7 nM
1h-79-1505 (SEQ ID NO:112)	103 ± 29 nM	-----
1h-79-1512 (SEQ ID NO:113)	19 ± 2 nM	9 ± 6 nM
1h-79-1519 (SEQ ID NO:114)	97 ± 18 nM	37 ± 36 nM
1h-79-1520 (SEQ ID NO:115)	113 ± 30 nM	68 ± 4 nM
1h-79-17 (SEQ ID NO:117)	2.5 ± 0.2 μM	-----
1h-79-2 (SEQ ID NO:120)	166 ± 47 nM	-----
1h-79-20 (SEQ ID NO:121)	1.8 ± 0.6 μM	-----

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-79-21 (SEQ ID NO:122)	3 ± 1 μM	-----
1h-79-22 (SEQ ID NO:123)	750 ± 212 nM	-----
1h-79-24 (SEQ ID NO:125)	331 ± 104 nM	295 ± 115 nM
1h-79-26 (SEQ ID NO:127)	62 ± 11 nM	38 ± 20 nM
1h-79-28 (SEQ ID NO:129)	40 nM	109 ± 59 nM
1h-79-29 (SEQ ID NO:130)	43 ± 9 nM	150 ± 89 nM
1h-79-30 (SEQ ID NO:132)	224 ± 54 nM	126 ± 29 nM
1h-79-31 (SEQ ID NO:133)	141 ± 62 nM	103 ± 56 nM
1h-79-32 (SEQ ID NO:134)	68 ± 6 nM	-----
1h-79-8 (SEQ ID NO:139)	240 ± 6 nM	-----
1h-79-802 (SEQ ID NO:141)	421 ± 147 nM	48 ± 8 nM
1h-79-806 (SEQ ID NO:145)	40 ± 3 nM	26 ± 8 nM
1h-79-807 (SEQ ID NO:146)	31 nM	53 ± 6 nM
1h-79-808 (SEQ ID NO:147)	560 ± 334 nM	-----
1h-79-809 (SEQ ID NO:148)	592 nM	-----
1h-80 (SEQ ID NO:156)	685 ± 370 nM	2 ± 0.4 μM
1h-80-1 (SEQ ID NO:157)	366 ± 56 nM	438 ± 370 nM
1h-80-2 (SEQ ID NO:161)	62 nM	550 ± 140 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-80-7 (SEQ ID NO:166)	322 ± 42 nM	-----
1h-81 (SEQ ID NO:169)	3.3 ± 2 μM	-----
1h-82 (SEQ ID NO:170)	1.9 ± 0.07 μM	-----
1h-83 (SEQ ID NO:171)	1.3 ± 0.5 μM	1.7 ± 1 μM
1h-84 (SEQ ID NO:172)	1.5 ± 0.4 μM	-----
1h-85 (SEQ ID NO:173)	530 ± 150 nM	-----
1h-86 (SEQ ID NO:174)	400 ± 0 nM	-----
1h-87 (SEQ ID NO:175)	1.7 ± 0.3 μM	-----
1h-90 (SEQ ID NO:178)	1.0 ± 0 μM	-----
1h-108 (SEQ ID NO:180)	1.9 ± 0 μM	2.7 ± 0.9 μM
1h-108-5 (SEQ ID NO:188)	1.9 ± 0 μM	-----
1h-109 (SEQ ID NO193:)	1 ± 0 μM	-----
1h-110 (SEQ ID NO194:)	4.1 ± 1 μM	-----
1h-112 (SEQ ID NO:397)	775 ± 430 nM	850 ± 320 nM
1h-116 (SEQ ID NO:196)	2.5 ± 1.9 μM	2.4 ± 1.2 μM
1h-203 (SEQ ID NO:200)	880 ± 140 nM	-----
1h-207 (SEQ ID NO:206)	2.6 μM	-----
1h-238 (SEQ ID NO:226)	775 ± 260 nM	-----

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-239 (SEQ ID NO:227)	1.3 ± 0.1 μM	-----
1h-239-8 (SEQ ID NO:228)	10 ± 4 nM	13 ± 3 nM
1h-239-804 (SEQ ID NO:229)	5 ± 2 nM	3 ± 2 nM
1h-239-807 (SEQ ID NO:230)	7 ± 2 nM	6 ± 1 nM
1h-239-809 (SEQ ID NO:231)	6 ± 1 nM	4 ± 1 nM
1h-239-815 (SEQ ID NO:232)	10 nM	6 ± 4 nM
1h-239-816 (SEQ ID NO:233)	11 ± 7 nM	13 ± 3 nM
1h-239-817 (SEQ ID NO:234)	7 nM	9 ± 2 nM
1h-239-819 (SEQ ID NO:235)	13 ± 5 nM	11 ± 8 nM
1h-239-824 (SEQ ID NO:236)	9 nM	6 ± 1 nM
1h-239-828 (SEQ ID NO:237)	8 nM	14 ± 6 nM
1h-239-829 (SEQ ID NO:238)	10 ± 3 nM	11 ± 2 nM
1h-239-832 (SEQ ID NO:239)	12 ± 6 nM	11 ± 6 nM
1h-239-833 (SEQ ID NO:240)	8 ± 1 nM	7 ± 0.7 nM
1h-239-837 (SEQ ID NO:241)	9 ± 1 nM	14 ± 6 nM
1h-239-838 (SEQ ID NO:242)	4 ± 0.6 nM	3 ± 2 nM
1h-239-840 (SEQ ID NO:243)	9 nM	10 ± 1 nM
1h-239-847 (SEQ ID NO:244)	8 ± 3 nM	5 ± 3 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-239-849 (SEQ ID NO:245)	13 ± 4 nM	10 ± 7 nM
1h-239-850 (SEQ ID NO:246)	9 ± 6 nM	2 ± 1 nM
1h-239-851 (SEQ ID NO:247)	5 nM	4 ± 0.7 nM
1h-239-856 (SEQ ID NO:248)	3 nM	1 nM
1h-239-857 (SEQ ID NO:249)	3 ± 0.7 nM	1 nM
1h-239-859 (SEQ ID NO:250)	5 ± 0.6 nM	4 ± 1 nM
1h-239-869 (SEQ ID NO:255)	-----	2 ± 0 nM
1h-239-870 (SEQ ID NO:256)	-----	3 ± 0.7 nM
1h-239-871 (SEQ ID NO:257)	-----	3 ± 0 nM
1h-239-9 (SEQ ID NO:271)	27 ± 6 nM	57 ± 13 nM
1h-239-872 (SEQ ID NO:258)	0.6	0.5 ± 0.2
1h-239-873 (SEQ ID NO:259)	1.4 ± 0.1	1 ± 0
1h-239-874 (SEQ ID NO:260)	-----	2 ± 0
1h-239-875 (SEQ ID NO:261)	0.8 ± 0.1	0.9 ± 0.6
1h-239-876 (SEQ ID NO:262)	1.2 ± 1	1.8 ± 1.4
1h-239-877 (SEQ ID NO:263)	2.2 ± 0.3	2 ± 0
1h-239-879 (SEQ ID NO:264)	1 ± 0	1.3 ± 0.9
1h-239-880 (SEQ ID NO:265)	0.8 ± 0.2	0.6 ± 0.2

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-239-881 (SEQ ID NO:266)	1 ± 0	1.3 ± 0.9
1h-239-882 (SEQ ID NO:267)	0.5 ± 0.1	0.5 ± 0.3
1h-239-883 (SEQ ID NO:268)	1.5 ± 0.7	1 ± 0.5
1h-239-885 (SEQ ID NO:269)	1.2 ± 0.4	0.9 ± 0.6
1h-239-886 (SEQ ID NO:270)	0.8 ± 0.1	0.9 ± 0.6
1h-239-887 (SEQ ID NO:472)	0.2	1 ± 0.7
1h-239-888 (SEQ ID NO:473)	1.7	62 ± 43
1h-239-889 (SEQ ID NO:474)	0.2	0.7 ± 0.5
1h-239-890 (SEQ ID NO:475)	0.2	0.7 ± 0.5
1h-239-891 (SEQ ID NO:476)	0.2	0.5 ± 0.3
1h-239-892 (SEQ ID NO:477)	0.3	0.6 ± 0.2
1h-239-893 (SEQ ID NO:478)	0.4	0.6 ± 0.2
1h-239-894 (SEQ ID NO:479)	0.4	0.3 ± 0.3
1h-239-895 (SEQ ID NO:480)	0.3	0.8 ± 0.3
1h-239-896 (SEQ ID NO:481)	0.2	0.5 ± 0.05
1h-239-897 (SEQ ID NO:482)	0.4	0.6 ± 0.2
1h-239-898 (SEQ ID NO:483)	0.5	0.8 ± 0.2

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-239-89103 (SEQ ID NO:534)	-----	0.7 ± 0.2
1h-239-89104 (SEQ ID NO:535)	-----	0.8 ± 0.3
1h-239-89201 (SEQ ID NO:547)	-----	0.6 ±0.1
1h-239-89202 (SEQ ID NO:548)	-----	2 ± 0
1h-239-89204 (SEQ ID NO:550)	-----	0.9 ± 0.2
1h-239-89205 (SEQ ID NO:551)	-----	0.6 ± 0.3
1h-239-89207 (SEQ ID NO:553)	-----	0.5 ± 0.2
1h-239-89216 (SEQ ID NO:562)	-----	0.8 ± 0.2
1h-239-89230 (SEQ ID NO:567)	-----	1.8 ± 0.3
1h-239-89233 (SEQ ID NO:570)	-----	0.8 ± 0.3
1h-239-89221 (SEQ ID NO:575)	-----	0.9 ± 0.3
1h-239-89222 (SEQ ID NO:576)	-----	0.9 ± 0.2
1h-239-89223 (SEQ ID NO:577)	-----	0.9 ± 0.2
1h-239-89224 (SEQ ID NO:578)	-----	1.6 ± 0.8
1h-239-89226 (SEQ ID NO:580)	-----	0.8 ± 0.3
VH dAbs		
1h-99-237 (SEQ ID NO:272)	3 ± 0.8 nM	3 ± 1.8 nM
1h-99-238 (SEQ ID NO:273)	3 ± 1 nM	5 ± 2 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-37 (SEQ ID NO:274)	1.3 ± 0.6 μM	1.9 ± 0.8 μM
1h-93 (SEQ ID NO:275)	2.8 ± 0.9 μM	3.2 ± 0.7 μM
1h-99 (SEQ ID NO:276)	3.2 ± 0.1 μM	2.2 ± 0.8 μM
1h-29 (SEQ ID NO:281)	>7 μM	-----
1h-30 (SEQ ID NO:282)	1.2 ± 0 μM	-----
1h-37 (SEQ ID NO:283)	1.3 ± 0.6 μM	1.9 ± 0.8 μM
1h-93 (SEQ ID NO:287)	2.8 ± 0.9 μM	3.2 ± 0.7 μM
1h-93-1 (SEQ ID NO:288)	493 ± 26 nM	545 ± 224 nM
1h-93-2 (SEQ ID NO:289)	383 ± 80 nM	830 ± 165 nM
1h-93-201 (SEQ ID NO:290)	182 ± 58 nM	18 ± 8 nM
1h-93-204 (SEQ ID NO:291)	176 ± 79 nM	1.2 ± 1.4 μM
1h-99 (SEQ ID NO:297)	3.2 ± 0.1 μM	2.2 ± 0.8 μM
1h-99-1 (SEQ ID NO:298)	15 ± 0 nM	19 ± 14 nM
1h-99-2 (SEQ ID NO:299)	17 ± 2 nM	13 ± 6 nM
1h-99-201 (SEQ ID NO:300)	14 ± 4 nM	18 ± 1 nM
1h-99-203 (SEQ ID NO:301)	8 ± 0 nM	10 ± 0 nM
1h-99-2112 (SEQ ID NO:311)	3 ± 1 nM	2 ± 1 nM
1h-99-2113 (SEQ ID NO:312)	5 ± 2 nM	3 ± 1 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-99-2114 (SEQ ID NO:313)	4 ± 1 nM	2 ± 1 nM
1h-99-2115 (SEQ ID NO:314)	3 ± 2 nM	12 ± 4 nM
1h-99-2116 (SEQ ID NO:315)	5 ± 2 nM	4 ± 1 nM
1h-99-217 (SEQ ID NO:320)	12 ± 2 nM	15 ± 2 nM
1h-99-218 (SEQ ID NO:321)	10 ± 2 nM	12 ± 1 nM
1h-99-220 (SEQ ID NO:323)	10 ± 1 nM	12 ± 1 nM
1h-99-221 (SEQ ID NO:324)	12 ± 1 nM	17 ± 4 nM
1h-99-222 (SEQ ID NO:325)	16 ± 2 nM	28 ± 16 nM
1h-99-224 (SEQ ID NO:327)	15 ± 1 nM	28 ± 9 nM
1h-99-225 (SEQ ID NO:328)	14 ± 4 nM	28 ± 12 nM
1h-99-226 (SEQ ID NO:329)	10 ± 1 nM	23 ± 2 nM
1h-99-227 (SEQ ID NO:330)	18 ± 3 nM	33 ± 18 nM
1h-99-228 (SEQ ID NO:331)	12 ± 8 nM	46 ± 6 nM
1h-99-229 (SEQ ID NO:332)	15 ± 3 nM	24 ± 4 nM
1h-99-230 (SEQ ID NO:333)	9 ± 1 nM	14 ± 6 nM
1h-99-236 (SEQ ID NO:339)	21 ± 6 nM	14 ± 9 nM
1h-99-237 (SEQ ID NO:340)	3 ± 1 nM	3 ± 2 nM
1h-99-238 (SEQ ID NO:341)	3 ± 1 nM	5 ± 2 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-99-241 (SEQ ID NO:342)	17 ± 1 nM	22 nM
1h-99-243 (SEQ ID NO:343)	4 ± 2 nM	8 ± 1 nM
1h-99-245 (SEQ ID NO:345)	6 ± 1 nM	11 ± 1 nM
1h-99-246 (SEQ ID NO:346)	3 ± 1 nM	8 ± 1 nM
1h-99-249 (SEQ ID NO:349)	6 ± 2 nM	11 ± 2 nM
1h-99-250 (SEQ ID NO:350)	9 ± 0 nM	8 nM
1h-99-254 (SEQ ID NO:354)	11 ± 1 nM	7 nM
1h-99-256 (SEQ ID NO:356)	9 ± 1 nM	7 ± 4 nM
1h-99-260 (SEQ ID NO:360)	11 ± 0 nM	13 nM
1h-99-262 (SEQ ID NO:398)	6 ± 2 nM	8 ± 4 nM
1h-99-263 (SEQ ID NO:362)	6 ± 1 nM	4 ± 2 nM
1h-99-264 (SEQ ID NO:363)	5 ± 2 nM	3 ± 2 nM
1h-99-265 (SEQ ID NO:364)	4 ± 1 nM	3 ± 1 nM
1h-99-266 (SEQ ID NO:365)	8 ± 4 nM	4 ± 1 nM
1h-99-267 (SEQ ID NO:366)	6 ± 3 nM	4 ± 1 nM
1h-99-268 (SEQ ID NO:367)	11 ± 2 nM	13 ± 1 nM
1h-99-269 (SEQ ID NO:368)	10 ± 2 nM	5 ± 0 nM
1h-99-270 (SEQ ID NO:369)	4 ± 2 nM	6 ± 2 nM

dAb	Luciferase assay (EC_{50})	MLR assay (EC_{50})
1h-99-275 (SEQ ID NO:370)	6 ± 1 nM	10 ± 3 nM
1h-99-276 (SEQ ID NO:371)	5 ± 1 nM	18 ± 1 nM
1h-99-277 (SEQ ID NO:372)	6 ± 2 nM	9 ± 1 nM
1h-99-278 (SEQ ID NO:373)	12 ± 2 nM	13 ± 1 nM
1h-99-297 (SEQ ID NO:374)	6 ± 1 nM	6 ± 0 nM
1h-100 (SEQ ID NO:380)	> 7 μM	-----
1h-114 (SEQ ID NO:388)	3.1 ± 1.4 μM	-----
1h-115 (SEQ ID NO:389)	4 ± 1.6 μM	> 7 μM
1h-119 (SEQ ID NO:392)	2.8 μM	-----
1h-212 (SEQ ID NO:393)	>7 μM	-----
1h-99-23703 (SEQ ID NO:599)	-----	7 ± 3
1h-99-23704 (SEQ ID NO:600)	-----	10 ± 1.4
1h-99-23711 (SEQ ID NO:607)	-----	11 ± 2.6
1h-99-23715 (SEQ ID NO:611)	-----	3.8 ± 1.3
1h-99-23721 (SEQ ID NO:617)	-----	6.3 ± 2.8
1h-99-23726 (SEQ ID NO:622)	-----	7.8 ± 3.2

Example 6: Polyethylene glycol modification of dAbs

PEGylation of various dAbs was undertaken to increase the stability, half-life, and bioavailability of dAbs set forth herein. For poly (ethylene glycol) (PEG)-modification

("PEGylation") of the N-terminal amine of dAbs, samples were purified and dialysed into phosphate-buffered saline (PBS) and the endotoxin levels in the solution were reduced to a maximum of 10 endotoxin units (EU)/mg (1 EU = 100 pg lipopolysaccharide). Samples were then dialysed into 0.1 M potassium phosphate pH 6.8. Samples were filtered after dialysis, the protein concentration determined and adjusted to 2-3mg/ml.

For the attachment of PEG (40kD linear, 40kD branched or 30 kD linear), a methoxy poly (ethylene glycol) propionaldehyde solid was added to solution in a 3 fold molar excess over dAb and mixed on a roller for 1 hour at room temperature. At that time, a 10-fold molar excess of sodium cyanoborohydride (from 5 mg/ml stock in 0.1M potassium phosphate pH 6.8) was added and mixed on a roller for 5 hours at room temperature. An additional 10-fold molar excess of sodium cyanoborhydride was added and the reaction allowed to proceed overnight at room temperature. The progression of PEGylation was monitored by SDS-PAGE.

For PEGylation of a cysteine residue in a dAb, either at the C-terminal position or at an internal position (e.g., amino acid position 15, 41, 60, 70, 81, or 100), dAbs were purified and dialysed into PBS, and endotoxin levels reduced to a maximum of 10 EU/mg. Samples were filtered after dialysis, and the dAb concentration determined and adjusted to 2-3 mg/ml.

For the attachment of PEG (40kD linear, 40kD branched or 30 kD linear), reduction of the dAb with dithiothreitol (DTT) was employed. Glycerol was added to the sample (20% (v/v)) and the sample thoroughly mixed before reduction with dithiothreitol (5 mM). The reaction was allowed to proceed at room temperature for 20 minutes before exchanging buffer into a PEG-coupling buffer (20 mM BIS-Tris pH 6.5, 5 mM EDTA and 10% glycerol [v/v]) using 26/10 Hi-Prep desalting column (GE Healthcare). The protein concentration was measured and adjusted to 2-3 mg/ml. Methoxy poly (ethylene glycol) maleimide solid was added to the solution in a 3 fold molar excess over the dAb and the solution mixed on a roller between 4 and 16 hours at room temperature. The progression of PEGylation was monitored by SDS-PAGE.

PEGylation was also carried out using reduction of the dAb with tris(2-carboxyethyl)phosphine (TCEP). The sample was dialyzed into PEG coupling buffer (20 mM BIS-Tris pH 6.5, 5 mM EDTA and 10% glycerol [v/v]) using a 26/10 HiPrep Desalting column (GE Healthcare). The concentration of dAb was measured and

adjusted to 2-3 mg/ml. Reduction was carried out using TCEP, added at a concentration of 5 mM, for 20 minutes at room temperature. A methoxy poly (ethylene glycol) maliemide solid was then added in a 3-fold molar excess over the dAb and mixed on a roller for 4-16 hours at room temperature. The progression of PEGylation was monitored by SDS-PAGE.

When required, maleimide was used to block cysteine residues. Protein samples were purified and dialysed into PBS and endotoxin levels reduced to a maximum of 10 EU/mg.

Samples were filtered after dialysis, and the protein concentration determined and adjusted to 2-3 mg/ml. For the addition of PEG, glycerol was added to the sample (20% (v/v) and thoroughly mixed before reduction with dithiothreitol (DTT 5mM). The reaction was allowed to proceed at room temperature for 20 minutes before dialysis into PEG coupling buffer (20 mM BIS-Tris pH 6.5, 5 mM EDTA and 10% glycerol [v/v],) using 26/10 Hi-Prep Desalting column (GE Healthcare). The protein concentration was measured and adjusted to 2-3 mg/ml. Maleimide solid was added in a 3-fold molar excess over dAb and mixed using a roller for 4-16 hours at room temperature. The extent of the reaction was monitored using SDS-PAGE.

The method used for purification of PEGylated dAbs depends on the isoelectric point (pI) of the dAb. For dAbs with a pI lower than 7, anion exchange was used, whereas for dAbs with a pI higher than 7, cation exchange was appropriate.

For purification, dAbs were first diluted 1:5 with Buffer A (20 mM Tris pH 8 for anion exchange and 20 mM Sodium acetate pH 4 for cation exchange) and the pH checked. Resource Q (anion exchanger) and S (cation exchanger), or HiTrap Q or S Fast Flow columns (GE Healthcare) were used. The columns were washed with 10 column volumes 0.5 M NaOH, followed by 10 column volumes of Buffer B (20 mM Tris pH 8, using 1 M NaCl for anion exchange and 20 mM sodium acetate pH 4, using 1 M NaCl for cation exchange). The columns were equilibrated with Buffer A before loading of the diluted sample. Elution of the sample was carried out over the following gradients:

0 – 30% Buffer B over 30 column volumes,

30-100% Buffer B over 10 column volumes,

100% Buffer B over 5 column volumes.

Any excess free PEG or maliemide passed through the column and remained in the flow through. The PEGylated sample usually eluted in the first gradient and was well separated from the second gradient where the remaining un-PEGylated sample eluted. Two-milliliter fractions were collected throughout each gradient and are analyzed by SDS-PAGE. The columns were finally washed with 0.5 M NaOH to elute any remaining material. Appropriate fractions were pooled and, in the case of high-pI dAbs, the pH adjusted to neutral by addition of 1 M Tris, pH 8.

Tables 2 and 3 demonstrate that PEGylated dAbs retain binding activity and biological activity in the assays used herein.

Table 2: Activity of PEGylated human dAbs.

Human CD28 dAb	Luciferase assay (EC_{50} nM)	DC-MLR Assay (EC_{50} nM)
1h-99-2	17 ± 2	13 ± 6
1h-99-2 40K linear PEG	100 ± 29	390 ± 145
1h-99.2 40K branched PEG	117	383 ± 21
1h-99-237	3 ± 1	3 ± 2
1h-99-237 40K linear PEG	------	2 ± 0
1h-99-238	3 ± 1	5 ± 2
1h-99-238 40K linear PEG	4.5 ± 1	29 ± 8
1h-239-8	10 ± 4	13 ± 3
1h-239-8 40K linear PEG	510 ± 100	285
1h-239-850	9 ± 6	2 ± 1
1h-239-850 40K linear PEG	2	4 ± 0
1h-239-891	0.2	0.5 ± 0.3
1h-239-891(Q3C)	------	1.5 ± 0.5

Human CD28 dAb	Luciferase assay (EC_{50} nM)	DC-MLR Assay (EC_{50} nM)
40K branched PEG		
1h-239-891(S9C) 40K branched PEG	------	1.3 ± 0.5
1h-239-891(G41C) 40K branched PEG	------	2 ± 0
1h-239-891(K42C) 40K branched PEG	------	13 ± 6
1h-239-891(S60C) 30K linear PEG	------	0.8 ± 0.3
1h-239-891(S60C) 40K branched PEG	------	1.2 ± 0.6
1h-239-891(D70C) 30K linear	------	1.2 ± 0.5
1h-239-891(D70C) 40K branched	------	2.3 ± 1.8
1h-239-891(Q79C) 40K branched PEG	------	4.9 ± 1.9

Table 3: Activity of PEGylated mouse dAb

mouse CD28 dAb	MLR Assay (EC_{50} nM)
74-15	11 ± 5
74-15 40K linear PEG	20 ± 1

Example 7: Animal Cross-Reactivity Studies with dAbs

The ability of dAbs set forth herein to react with non-human cells and polypeptides was examined. In a cross-reactivity study, dAb 1h-79-807 demonstrated activity against both human and mouse cells expressing CD28. For the human cell study, the luciferase and MLR assays were used, as described above. For the mouse cell study, MLR and mouse splenocyte assays were used. In the assays, dAb 1h-79-807

exhibited a potency of 31 +/- 12 nM (splenocyte assay) and a potency of 38 +/- 6 nM (MLR assay).

For the mouse MLR assays, single cell suspensions were made from lymph nodes of a BALB\c mouse and spleens from a DBA\2 mouse using a Tenbroeck tissue homogenizer. The red blood cells were removed from both populations through lysis using Red Blood Cell Lysis buffer (SIGMA, St Louis, Mo), followed by two washes in complete media [(RPMI 1640 (Invitrogen, Carlsbad, CA), 10% Fetal Calf Serum (Summit), 1% l-glutamine (Invitrogen), 1% sodium pyruvate (Invitrogen), 100 μg/ml gentamicin (Invitrogen), $5x10^{-5}$ M 2-mercaptoethanol (SIGMA)]. After the final wash, the cell pellets were resuspended in 2 ml of complete media, loaded onto individual pre-equilibrated nylon wool columns (WAKO, Richmond, VA), and incubated at 37°C for 60 min. The T cells from either the BALB/c lymph node and DBA\2 spleens were eluted from the column by the addition of 25 ml of warm media. The T cells from the DBA\2 spleens were discarded, and the APC population eluted from the column with the addition of 25 ml of ice cold complete media (describe *supra*). The BALB\c T cells or the DBA/2 APCs were centrifuged at 400xg for 10 minutes, resuspended in complete media, and the cells counted on a hemacytometer. Both cell populations were diluted to $1.0x10^6$ cells/ml in complete media. DBA\2 APCs ($0.25x10^6$ /ml) were combined with BALB\c T cells ($0.5x10^6$ /ml) in a round-bottom 96-well plate (Becton Dickinson, Franklin Lakes, NJ), and serial dilutions of dAb, or control agent, was added to the wells. The plates were incubated at 37°C in 5% CO_2 for 96 hours. ^{3}H-thymidine (1 μCi; PerkinElmer, Waltham, MA) was added to the wells 6 hours prior to the end of the incubation period. Plates were harvested through GF/c filter plates (PerkinElmer), dried, then 50 μl of Microscint-20 (PerkinElmer) added to each well, and radioactivity counted on a TopCount (Packard, Meriden, CT). Data was analyzed using the ExcelFit program (Microsoft, Redmond, WA).

For the mouse spleno cyte assay, single cell suspensions were generated from spleens of BALB\c mice using a Tenbroeck tissue homogenizer. The red blood cells were separated from other homogenate matter by incubation in Red Blood Cell Lysis buffer, followed by two washes in complete media [RPMI 1640 (Invitrogen), 10% Fetal Calf Serum (Summit), 1% l-glutamine (Invitrogen), 1% Sodium Pyruvate (Invitrogen), 100 μg/ml gentamicin (Invitrogen), $5x10^{-5}$M 2-mercaptoethanol (SIGMA)]. After the final wash, the cell pellet was resuspended in complete media and splenocytes counted

using a hemacytometer. The splenocytes were diluted to $1.0x10^6$ cells/ml in complete medium, and 500 µl added to round-bottom 96-well plates. Anti-CD3 antibody (clone 145-2C11 (BMS)) was added to each well at a concentration of 0.1 µg/ml. Serial dilutions of dAb, or control agents, were added to the wells, incubated at 37°C in 5% CO_2 for 48 hours. ^{3}H-thymidine (1 µCi) was added to the wells 6 hours prior to the end of the incubation period, and the splenocytes harvested through GF/c filter plates (PerkinElmer). The plates were dried, 50 µl of Microscint-20 (PerkinElmer) was added to each well, and radioactivity counted on a TopCount. Data was analyzed using the ExcelFit program.

In another cross-reactivity study, the pharmacokinetics (PK) of dAbs were examined using Cynomolgus monkeys, in order to elucidate the PK in relation to size and conformation of polyethylene glycol (PEG)-modified ("PEGylated") dAbs. The effect of anti-human CD28 dAb 1h 99-2-PEG, bearing a 40 kD PEG moiety, was examined in two groups, each containing three monkeys. Group 1 monkeys received dAb 1h 99-2 P40-Branched PEG subcutaneously, at a concentration of 10 mg/kg. Group 2 monkeys received dAb 1h 99-2 P40-Linear PEG subcutaneously, at a concentration of 10 mg/kg. All serum samples collected from animals were stored at -70° C and analyzed at the conclusion of the study. Serum samples were analyzed using ELISA and MSD at several dilutions.

For the ELISA analysis, biotin-monomeric CD28 was coated on an ELISA plates at a concentration of 1 µg/ml. Standards, quality control samples, and all experimental sample dilutions were prepared at final serum concentration of 1%. Cynomolgus samples were thawed at room temperature and several dilutions of the samples were prepared to identify signals within the assay range. Cynomolgus samples were added to the wells on the ELISA plate and incubated for two hours at room temperature. Rabbit anti-Vh dAbs were prepared and isolated using affinity purification and a polyclonal antibody. Donkey anti-rabbit – HRP was added to the plates, followed by substrate, and after the reaction proceeded for a measured amount of time, the reaction was stopped. The optical density (OD) of the each reaction was measured using a microplate optical reader. A standard curve was generated, and a four-parameter logistic fit of the standard curve was used to calculate dAb concentrations in the wells based on the OD readings within the quantifiable range. Results were based on an average of concentrations from multiple dilutions.

Tables 4-6 describe the results obtained from the administration of dAb 1h 99-2 P40-Branched and dAb 1h 99-2 P40-Linear to Cynomolgus monkeys. FIG. 5 illustrates the plasma concentration, over time, of the study of the PEGylated dAbs in the monkeys.

The experimental results with branched PEGylated dAb differed from those for the linear PEGylated dAb in both exposure and terminal half-life, which may be due to the difference in absorption rather than disposition.

Although the half-life ($T_{1/2}$) of the branched dAb ($T_{1/2}$ = 4.5 days) appeared to be shorter than that of the linear dAb ($T_{1/2}$ = 6 days), the branched-PEG dAb is a better candidate in terms of exposure and potential coverage over the target concentration (e.g., the *in vitro* IC_{50} = 3 μg/mL or 200 nM). The AUC of the branched dAb was ~ 2.5 fold greater than that of the linear dAb (single factor Anova P = 0.017). The mean residence time (MRT) of the branched dAb was ~ 1.5 fold higher than that of linear dAb.

After subcutaneous administration, the peak concentrations of both PEGylated proteins occurred around 24 hours. The steady state volume of distribution (Vss/F) values for both dAbs were below 100 mL/kg, indicating that the PEGylated proteins largely reside in the plasma.

Table 4: Serum levels of dAb 1h 99-2 P40-Branched

Group 1: 1h 99-2 p40Br (μg/ml)

Hours post dose	Monkey #				
	1101	1102	1103	MEAN	SD
1	0.592	2.916	0.671	1.39	1.32
2	3.398	7.989	2.839	4.74	2.83
4	28.494	17.417	12.747	19.55	8.09
8	75.129	61.516	40.057	58.90	17.68
12	80.598	82.753	44.651	69.33	21.40
24	174.252	144.025	107.507	141.93	33.42
96	125.813	109.162	107.421	114.13	10.15
168	71.762	111.085	49.670	77.51	31.11
240	45.573	68.400	32.332	48.77	18.25
336	22.922	45.246	16.363	28.18	15.14
504	7.441	10.925	3.379	7.25	3.78

672	2.187	5.836	1.204	3.08	2.44
840	0.810	1.861	0.747	1.14	0.63

Table 5: Serum levels of dAb 1h 99-2 P40-Linear

	Group 2: 1h 99-2 P40L (µg/ml)				
Hours post dose	Monkey #				
	2101	2102	2103	MEAN	SD
1	1.335	0.137	1.524	1.00	0.75
2	5.540	1.427	5.500	4.16	2.36
4	15.190	5.990	15.062	12.08	5.28
8	42.403	26.227	61.192	43.27	17.50
12	67.873	31.246	67.810	55.64	21.13
24	111.762	82.306	107.172	100.41	15.85
96	57.389	55.502	58.679	57.19	1.60
168	23.335	31.518	26.847	27.23	4.11
240	7.744	11.258	8.730	9.24	1.81
336	2.946	3.276	3.895	3.37	0.48
504	0.850	1.303	1.131	1.09	0.23
672	0.394	0.693	0.542	0.54	0.15
840	0.202	0.275	0.197	0.22	0.04

Table 6: Summary of pharmacokinetic (PK) parameters for PEGylated dAbs

		Group 1: 1h-99-2 P40Br		**Group 2: 1h-99-2 P40L**	
Study	Unit	Mean	SD	Mean	SD
Dose	mg/kg	10		10	
Cmax	µg/mL	141.9	33.42	100.4	15.85
Tmax	h	24	0	24	0
AUClast	µg/ml*h	29414	7618	11978	531.4
AUCtot	µg/ml*h	29576	7730	12024	518.7
T1/2	h	105.41	7.80	142.2	21.04
MRT	h	174.13	27.25	117.1	11.98
Clearance/F	mL/min/kg	0.00592	0.002	0.0139	0.0006
Vss/F	mL/kg	60.43	10.54	97.69	13.56

The data in Experimental Example 7, as well as in Tables 4-6 demonstrates that dAbs set forth herein are cross-reactive human, mouse, and monkey model systems. Furthermore, the pharmacokinetic parameters for PEGylated dAbs demonstrate that the dAbs are bioavailable and active in living subjects.

Example 8: Method for SEC-MALLS analysis of dAbs

In order to estimate solution size and oligomeric structure of dAbs, multi-angle laser light scattering was used in conjunction with size-exclusion chromatography. Polypeptide samples were purified and dialysed into appropriate buffer (i.e., PBS). Samples were filtered after dialysis, concentration determined and adjusted to 1 mg/ml. BSA was purchased from Sigma and used without further purification.

A Shimadzu LC-20AD Prominence HPLC system with an autosampler (SIL-20A) and SPD-20A Prominence UV/Visible light detector was connected to Wyatt Mini Dawn Treos (MALLS, multi-angle laser light scattering detector) and Wyatt Optilab rEX DRI (differential refractive index) detector. The detectors were connected in the following order – LS-UV-RI. Both RI and LS instruments operated at a wavelength of 488 nm. TSK2000 (Tosoh corporation) or BioSep2000 (Phenomenex) columns were used (both are silica-based HPLC columns with similar separation range, 1-300 kD) with mobile phase of 50 mM phosphate buffer (with or without salt), pH 7.4 or 1x PBS. To improve recovery of the protein from the column, 10% ethanol was sometimes added. The flow rate used was either 0.5 or 1.0 ml/min, and the time course of the run was adjusted to reflect different flow rates (45 or 23 minutes) and was not expected to have significant impact onto separation of the molecules. Proteins were prepared in PBS to a concentration of 1 mg/ml and the injection volume was 100 µl.

The light-scattering detector was calibrated with toluene according to the manufacturer's instructions. The UV detector output and RI detector output were connected to the light scattering instrument so that the signals from all three detectors could be simultaneously collected with the Wyatt ASTRA software. Several injections of BSA in a mobile phase of PBS (0.5 or 1 ml/min.) were run over a Tosoh TSK2000 column with UV, LS and RI signals collected by the Wyatt software. The traces are then analyzed using ASTRA software, and the signals were normalized aligned and corrected for band broadening following manufacturer's instructions. Calibration constants were then averaged and input into the template which is used for future sample runs.

Absolute Molar Mass Calculations

One hundred microliters of 1 mg/ml sample were injected onto appropriate pre-equilibrated column. After processing through the SEC column, the sample passed through 3 on-line detectors – UV, MALLS (multi-angle laser light scattering) and DRI (differential refractive index), allowing absolute molar mass determination. The dilution that takes place on the column is about 10-fold, so the concentration at which in-solution state was determined was 100 μg/ml, or about 8uM dAb.

The basis of the calculations in ASTRA as well as of the Zimm plot technique, which is often implemented in a batch sample mode is the equation from Zimm (1948) *J. Chem. Phys.* 16:1093–1099:

$$\frac{R\theta}{K^*C} = MP(\theta) - 2A_2cM^2P^2(\theta) \qquad \text{(Eq. 1)}$$

wherein

- c is the mass concentration of the solute molecules in the solvent (g/mL)
- M is the weight average molar mass (g/mol)
- A_2 is the second virial coefficient (mol mL / g^2)
- $K^* = 4p^2 n_0^2 (dn/dc)^2 l_0^{-4} N_A^{-1}$ is an optical constant where n_0 is the refractive index of the solvent at the incident radiation (vacuum) wavelength, l_0 is the incident radiation (vacuum) wavelength, expressed in nanometers, N_A is Avogadro's number, equal to 6.022×10^{23} mol^{-1}, and dn/dc is the differential refractive index increment of the solvent-solute solution with respect to a change in solute concentration, expressed in mL/g (this factor must be measured independently using a dRI detector).
- $P(q)$ is the theoretically-derived form factor, approximately equal to $1 - 2\mu^2\langle r^2\rangle / 3! + \ldots$, where $\mu = (4\pi/\lambda)\sin(\theta/2)$, and $\langle r^2\rangle$ is the mean square radius. $P(q)$ is a function of the molecules' z-average size, shape, and structure.
- R_q is the excess Rayleigh ratio (cm^{-1})

This equation assumes vertically polarized incident light and is valid to order c^2.

To perform calculations with the Zimm fit method, which is a fit to R_q/K^*c vs. $\sin^2(q/2)$, we need to expand the reciprocal of Eq. 1 first order in c:

To perform calculations with the Zimm fit method, which is a fit to Rq /K*c vs. sin2(q/2), we need to expand the reciprocal of Eq. 1 to first order in c:

$$\frac{K^x c}{R_\theta} = \frac{1}{MP(\theta)} + 2A_2c \qquad \text{(Eq. 2)}$$

The appropriate results in this case were

$$M = ([K^x c/R_0] - 2A_2c)^{-1} \qquad \text{(Eq. 3)}$$

and

$$\langle r^2 \rangle = \frac{3m_0\lambda^2 M}{16\pi^2} \qquad \text{(Eq. 4)}$$

where

$$m_0 = d[K^x c / R_\theta] / d[\sin^2(\theta/2)]_{\theta \to 0} \qquad \text{(Eq. 5).}$$

The calculations were performed automatically by ASTRA software, resulting in a plot with molar mass determined for each of the data slices. Molar mass values obtained from the plot for each of the peaks observed on chromatogram was compared with expected molecular mass of a single unit of the protein. This enables a determination of in-solution state of the protein.

Table 7: Solution State and Size of dAbs

dAb	SEC-MALLS	MW	Column & mobile phase
1h-35	Monomer/dimer equilibrium	20kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-36	Monomer	16kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-37	Monomer	15kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-79	Monomer/dimer equilibrium	21kD	TSK2000, PBS pH 7.4 10% Ethanol, 0.5ml/min
1h-80	Monomer/dimer equilibrium	17kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-83	Monomer	16kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-93	Monomer	16kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-99	Monomer/dimer equilibrium	19kD	BioSep 2000, PBS pH7.4, 0.5 ml/min
1h-108	Monomer	17kD	TSK2000, PBS pH 7.4 10% Ethanol, 0.5 ml/min

dAb	SEC-MALLS	MW	Column & mobile phase
1h-99-237	Monomer	12kD	TSK2000, PBS pH 7.4 10% Ethanol, 1.0 ml/min
1h-99-238	Monomer plus dimer	12 & 26kD	TSK2000, PBS pH 7.4 10% Ethanol, 1.0 ml/min
1h-239-850	Monomer/dimer equilibrium	21kD	TSK2000, PBS pH 7.4 10% Ethanol, 1.0 ml/min

Example 9: Anti-CD28 dAbs Inhibit Cytokine Production in the Context of a DC-Driven MLR

This example demonstrates that anti-CD28 domain antibodies are capable of inhibiting cytokine production in the context of a dendritic cell-driven MLR.

Peripheral blood mononuclear cells (PBMC) were obtained by density-gradient separation of whole blood from normal human donors. T cells were prepared from E^+ fractions of PBMC rosetted with sheep red blood cells (Colorado Serum Company). Dendritic cells (DCs) were generated by adherence of monocytes from E^- fractions of PBMC to plastic and culture with GM-CSF and IL-4 (Invitrogen) for 7 days, followed by the addition of LPS (Sigma, 1 μg/ml) for 24 hours to induce maturation. Anti-CD28 domain antibodies were titrated in half log dilutions for a nine point dose response curve to evaluate their inhibition of a 1:10 ratio of dendritic cell to T cell interaction. Cytokine production was measured in supernatants by commercial ELISA (R&D Systems). IL-2 and IFNγ were measured on day 2 after stimulation, and TNFα was measured on day 3. Proliferation was measured by ^{3}[H]-thymidine incorporation on day 5. EC_{50} values were generated from inhibition curves of each treatment. Results are shown in Table 8. "239-891-D70C P30L PEG" and "239-891-D70C P40B PEG" below stand for the anti-CD28 human Vκ domain antibody (dAb) 1h-239-891-D70C PEGylated with either a 30 kDa linear or 40 kDa branched polyethylene glycol, respectively.

Table 8

Anti-CD28 dAb	IL-2 (EC_{50} nM)	TNFα (EC_{50} nM)	IFNγ (EC_{50} nM)
	(n = 4)	(n = 6)	(n = 4)
99-265	2.4 ± 0.4	3.6 ± 0.6	4.6 ± 0.8

239-890	0.1 ± 0.03	0.2 ± 0.04	0.3 ± 0.14
239-891	0.1 ± 0.06	0.2 ± 0.06	0.2 ± 0.08
239-896	0.3 ± 0.04	0.3 ± 0.06	0.3 ± 0.05
	(n = 10)	(n = 10)	(n = 10)
239-891-D70C P30L PEG	0.6 ± 0.09	0.6 ± 0.1	0.6 ± 0.08
239-891-D70C P40B PEG	1.5 ± 0.2	1.7 ± 0.36	2.5 ± 0.5

Example 10: CD28 dAbs are Equally Effective in Inhibiting CD80 vs CD86-driven T Cell Proliferation

This example demonstrates that anti-CD28 domain antibodies inhibit both CD80- and CD86-driven T cell proliferation.

T cells were prepared from E^+ fractions of PBMC rosetted with sheep red blood cells. Chinese hamster ovary (CHO) cells stably transfected with either human CD80 or CD86 were combined with T cells in the presence of 1 μg/ml of αCD3 (OKT3). The anti-CD28 domain antibodies were titrated in half log dilutions for a nine point dose response curve to evaluate their inhibition of a 1:3 ratio of CD80- or CD86-CHO to T cell interaction. Proliferation was measured by ^{3}[H]-thymidine incorporation on day 5. EC_{50} values were generated from inhibition curves of each treatment. Results are shown in Table 9.

Table 9

dAb	CD80 CHO (EC_{50} nM)	CD86 CHO (EC_{50} nM)
239-891	0.3 ± 0.1 (n = 9)	0.4 ± 0.1 (n = 9)
239-891-D70C P30L PEG	1 ± 0.2 (n = 5)	0.5 ± 0.2 (n = 5)
239-891-D70C P40Br PEG	0.4 ± 0.05 (n = 5)	0.4 ± 0.05 (n = 5)

Example 11: CD28 dAbs Inhibit T Cell Proliferation Initiated By Different APCs

This example demonstrates that anti-CD28 domain antibodies inhibit T cell proliferation initiated by different antigen presenting cells.

T cells were prepared from E^+ fractions of PBMC rosetted with sheep red blood cells (Colorado Serum Company). Dendritic cells (DCs) were generated by adherence of monocytes from E^- fractions of PBMC to plastic and culture with GM-CSF and IL-4 (Invitrogen) for 7 days, followed by the addition of LPS (Sigma, 1 μg/ml) for 24 hours to induce maturation. Monocytes were prepared from E^- fractions of PBMC by elutriation. The lymphoblastoid cell line (PM-LCL) is an EBV-transformed B-cell line from a normal donor. The various APCs were combined with allogeneic T cells at a ratio of 1:50. Anti-CD28 domain antibodies were titrated in half log dilutions for a nine point dose response curve to evaluate their inhibition of proliferation, which was measured by ^{3}[H]-thymidine incorporation on day 5. EC_{50} values were generated from inhibition curves of each treatment. Results are shown in Table 10.

Table 10

dAb	DCs	LCL B cells	Monocytes
239-891 (n = 2)	0.2, 0.2	0.3, 0.1	0.2, 1.4
239-891-D70C P30L PEG	0.5 ± 0.1	0.8 ± 0.3	2.3 ± 0.8
239-891-D70C P40B PEG	1.2 ± 0.1	2.4 ± 0.4	10 ± 4

Example 12: Anti-CD28 Domain Antibodies Lack Agonist Activity

This example demonstrates that anti-CD28 domain antibodies lack agonist activity.

The anti-CD28 domain antibody 239-891-D70C and the mitogenic anti-human CD28 antibody 5.11A1 were separately titrated in half-log dilutions in PBS, coated in the bottom of 96-well round-bottom plates and allowed to air-dry. PBMC were isolated from whole blood of normal human donors and added to wells containing the air-dried antibodies. Proliferation was measured by ^{3}[H]-thymidine incorporation on day 3, as shown in FIG. 10A, and IL-2 production was measured, as shown in FIG. 10B.

Example 13: Anti-CD28 Domain Antibodies Bind Their Target *In Vivo* and Lack Agonist Activity

This example demonstrates that anti-CD28 domain antibodies bind their target *in vivo* and lack agonist activity.

Cynomolgus monkeys were administered a single subcutaneous dose of the anti-CD28 human Vκ domain antibody (dAb) 1h-239-891-D70C PEGylated with either a 30 kDa linear or 40 kDa branched polyethylene glycol (PEG).

CD28 receptor occupancy (RO) on peripheral-blood T-helper cells (CD3+CD4+CD8-) was monitored at 2, 4, 24, 48, 96, 168, 240, 336, 408, 504, and 672 hours postdose using flow cytometry. Up to 100% RO was observed and sustained for a duration that correlated with plasma drug concentrations.

Although non-human primates are not sensitive to cytokine release syndrome (CRS) per se (reviewed in Horvath and Milton, Toxicol. Pathol. 37(3): 372-383 (2009)), the presence of moderate increases in cytokine concentrations may be useful to predict CRS in humans. Thus, plasma cytokine concentrations (IL-1β, IL-2, IL-5, IL-6, IFN-γ, and TNF-α) were evaluated predose and at 2, 4, 8, and 24 hours postdose using a multiplex bead-based assay. No drug-related cytokine release was observed, with most cytokine concentrations falling below the limit of detection. The absence of even moderate effects of this dAb on plasma cytokine concentrations supports a lack of agonistic activity.

Due to the absence of CRS in nonhuman primates, monitoring of peripheral-blood T-cell counts might predict unwanted T cell activation and T cell depletion in humans (Horvath and Milton (2009) *Toxicol. Pathol.* 37(3): 372-83). Thus, peripheral-blood T-cell counts were monitored at 2, 4, 24, 48, 96, 168, 240, 336, 408, 504, and 672 hours postdose using flow cytometry. There were no rapid or profound changes in peripheral-blood T-cell counts akin to those observed in humans following a single-dose of the superagonistic monoclonal antibody TGN 1412 (Suntharalingam et al. (2006) *New Engl. J. Med.* 355(10): 1018-28) or in non-human primates following dosing with OKT3 and HuM291 (reviewed in Horvath and Milton, 2009). The lack of any rapid and/or profound effects of this dAb on peripheral-blood T-cell counts supports a lack of agonistic activity.

The disclosure set forth herein has been particularly shown and described with references to specific embodiments thereof. It will be understood by those skilled in the

art that various changes in form and details may be made therein without departing from the scope encompassed by the appended claims.

Claims:

1. An isolated antibody polypeptide that binds the same epitope as domain antibody (dAb) 1h-239-891(D70C) (SEQ ID NO: 543), wherein said antibody polypeptide comprises a variable domain having a binding specificity to CD28 and at least 90% sequence identity to the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543).

2. The antibody polypeptide of claim 1, wherein the antibody polypeptide is 1h-239-891(D70C) (SEQ ID NO: 543).

3. The antibody polypeptide of claim 1, wherein the antibody polypeptide comprises a first single variable domain having a binding specificity to a first antigen and a second single variable domain having a binding specificity to a second antigen, wherein the first antigen is CD28, and wherein the second antigen is an antigen to other than CD28.

4. The antibody of claim 3, wherein the second antigen is an antigen presenting cell surface antigen or a T cell surface antigen.

5. The antibody polypeptide of claim 3, wherein the second antigen is a cytokine.

6. A pharmaceutical composition comprising a therapeutically-effective amount of an antibody polypeptide of claim 1 and a pharmaceutically acceptable carrier.

7. The pharmaceutical composition of claim 6, further comprising an immunosuppressive/immunomodulatory and/or anti-inflammatory agent.

8. Use of the pharmaceutical composition of claim 6 in the manufacture of a medicament for treating or alleviating an autoimmune disease in a human individual in need of such treatment, wherein the autoimmune disease is treated or alleviated.

9. The use of claim 8, wherein the pharmaceutical composition is administered in combination with an immunosuppressive/immunomodulatory and/or anti-inflammatory agent.

10. The antibody polypeptide of claim 1, wherein said antibody polypeptide comprises a variable domain having at least 95% sequence identity to the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543).

11. The antibody polypeptide of claim 10, wherein said antibody polypeptide comprises a variable domain having the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543).

12. The antibody polypeptide of claim 1, wherein said antibody polypeptide comprises a variable domain that has a binding specificity to CD28 and that differs from the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543) by 10 or fewer amino acid positions.

13. The antibody polypeptide of claim 1, wherein said antibody polypeptide comprises a variable domain that has a binding specificity to CD28 and that differs from the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543) by 5 or fewer amino acid positions.

14. Use of the antibody polypeptide of claim 1 in the manufacture of a medicament for treating or alleviating an immune disease in a human individual in need of such treatment, wherein the immune disease is prevented, treated, or alleviated, and wherein the immune disease is a graft-related disease.

15. The use of claim 14, wherein the graft-related disease is an allograft rejection.

16. The use of claim 14, wherein the graft-related disease is a xenograft rejection.

17. The use of claim 14, wherein the graft-related disease is graft versus host disease (GVHD).

18. The use of claim 14, wherein the graft-related disease is an acute transplantation rejection.

19. The use of claim 14, wherein the graft-related disease is a chronic transplantation rejection.

20. The use of claim 14, wherein the antibody polypeptide is administered in combination with an immunosuppressive/immunomodulatory and/or anti-inflammatory agent.

21. The use of claim 14, wherein said antibody polypeptide comprises a variable domain having at least 95% sequence identity to the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543).

22. The use of claim 14, wherein said antibody polypeptide comprises a variable domain having the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543).

23. The use of claim 14, wherein said antibody polypeptide comprises a variable domain that has a binding specificity to CD28 and that differs from the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543) by 8 or fewer amino acid positions.

24. The use of claim 14, wherein said antibody polypeptide comprises a variable domain that has a binding specificity to CD28, and that differs from the amino acid sequence of dAb 1h-239-891(D70C) (SEQ ID NO: 543) by 3 or fewer amino acid positions.

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gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttaat cgttatgcga tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatgg attgatggta atggtctggt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacggact 300

aggtctcatt ctgattcggg ttgggctttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 18
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 18
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga ccgtgtcacc 60

atcacttgcc gggcaagtca gtatattggt acttcgttaa attggtacca gcagaaacca 120

gggaaagccc ctaagctcct gacctatcag gcttccttgt tgcaaagtgg ggtcccatca 180

cgtttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg ctacgtacta ctgtcaacag ttggcgctgc gtcctatgac gttcggccaa 300

gggaccaagg tggaaatcaa acggg 325

<210> 19
<211> 370
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 19
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt aattataata tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaggt attacgaagg gtggtcgggt gacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaattgggt 300

ccgtcgagga tgcttaatga gccgctgttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagcg 370

<210> 20
<211> 370
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 20
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttccg gcgtattcga tgatttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaacg atttcgccgc tgggttattc gacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc ggaacagacg 300

gcttatttga atcgtgctac ggagcatttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagcg 370

<210> 21
<211> 370
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 21
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttcg aagtatgata tggcttgggt ccgccaggct 120

ccagggaagg gtctggagtg ggtctcatcg atttatgcta ttggtggtaa tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaattgaag 300

tcggggatgc agactcggtt gaattctttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagcg 370

<210> 22
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 22
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgag ctgtatcaga tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaact attatgccta gtggtaatct tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaaatgtgg 300

tcgttgaatt tggggtttca tgcggctttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 23
<211> 370
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 23
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggg cagtatggta tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaggg attagtcctt ctggtaatta tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaagggaat 300

gggtctcttc cgcctcgtgg gtctattttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagcg 370

<210> 24
<211> 370
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 24
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt aattataata tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaggt attacgaagg gtggtcgggt gacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaattgggt 300

ccgtcgagga tgcttaatga gccgctgttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagcg 370

<210> 25
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 25
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggg acgtattata tggggtgggc ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatct attggggcta atggtgctcc tacatattac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaaattcgt 300

tcgcttaata ggtgggcgga gcctgtgttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 26
<211> 349
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 26
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgct gattattcta tgtattgggt ccgccaggct 120

ccagggaagg gtctggagtg ggtctcacag attagtccgg cgggttcttt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaagattct 300

aagtcttttg actactgggg tcagggaacc ctggtcaccg tctcgagcg 349

<210> 27
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 27
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga ccgtgtcacc 60

atcacttgcc gggcaagtca gagtattggg acgggtttac ggtggtacca gcagaaacca 120

gggaaagccc ctatgctcct gatctatcgg gcgtccattt tgcaaagtgg ggtcccatca 180

cgttttagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg ctacgtacta ctgtcaacag acgactcttc agccttttac gttcagccaa 300

gggactaagg tggaaatcaa acggg 325

<210> 28
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 28
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga ccgtgtcacc 60

atcacttgcc gggcaagtca gtctattagt cattcgttag tttggtacca gcagaaacca 120

gggaaagccc ctaagctcct gatctattgg gcttcccttt tgcaaagtgg ggtcccatca 180

cgtttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg ctacgtacta ctgtcaacag ggtatgacta cgcctttac gttcggccaa 300

gggaccaagg tggaaatcaa acggg 325

<210> 29
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 29
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgat agttatgata tgaattgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcacag atttctgctg atggtcattt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaatcgcgg 300

agtagttttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 30
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 30
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttagg gattatatga tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcacgt attgattctc atggtaatcg tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacatatg 300

acgggttttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 31
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 31
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttagg gagtatatga tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcacgt attaatggtg tgggtaattc tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacatcag 300

gtgggttttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 32
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 32
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttagt gattatatga tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcacgt attacgtctg agggttcgca tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacatacg 300

tctggttttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 33
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 33
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggg aggtatatga tggggtgggt ccgccaggct 120

ccagggaagg gtctggagtg ggtctcacgg atttctggtc ctggtacggt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacatgat 300

acggggtttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 34
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 34
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt caccttttct tcttatgcta tgatttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcagag atttctcctt atggtaatca tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacctgat 300

cggcgttttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 35
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 35
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttact tcgtatggga tgcagtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatcg atttctactg atggtatggt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaacttggg 300

gttaattttg actactgggg tcagggaacc ctggtcaccg tctcgagc 348

<210> 36
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 36
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt gattatatga tggggtgggt ccgccaggct 120

ccagggaagg gtctggagtg ggtctcaatt attcgtgtgc ctggttcgac tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacagaag 300

ggtgatgagt ttgactactg gggtcaggga accctggtca ccgtctcgag c 351

<210> 37
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 37
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttatt ctgtatgata tgcagtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcacgt atttctgcta atggtcatga tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaaggtccg 300

cattatttgt ttgactactg gggtcaggga accctggtca ccgtctcgag c 351

<210> 38
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 38
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgcgcag cctccggatt cacctttact aagtatttta tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcactg attgatccgc gtggtcctca tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacagttg 300

ggtgaggagt ttgactactg gggtcaggga accctggtca ccgtctcgag c 351

<210> 39
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 39
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttaag acttatacga tgaggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaact attaattcga gtggtacttt gacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaatctagt 300

tcttatacgt ttgactactg gggtcaggga accctggtca ccgtctcgag c 351

<210> 40
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 40
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgcg atgtatagta tgaagtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatcg atttcgaatg ctggtgatat tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc ggaatcgttt 300

aggtctcgtt attttgacta ctggggtcag ggaaccctgg tcaccgtctc gagc 354

<210> 41
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 41
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgat gattatctta tggggtgggt ccgccaggct 120

ccagggaagg gtctggagtg ggtctcactg attcgtatga ggggttctgt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacattct 300

cttactacta atctttttga ctactggggt cagggaaccc tggtcaccgt ctcgagc 357

<210> 42
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 42
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttact gattatatga tggcttgggc ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaatt attgggacta ctggtacgtg gacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaaactaat 300

gcgtatgaga gtgagtttga ctactggggt cagggaaccc tggtcaccgt ctcgagc 357

<210> 43
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 43
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgcg cggtatacta tggtgtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcagct attcattttg atggtcggac tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga atagcctgcg tgccgaggac accgcggtat attactgtgc gaaaaatgag 300

tgggcgtctc ttaagcattt tgactactgg ggtcagggaa ccctggtcac cgtctcgagc 360

<210> 44
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polynucleotide"

<400> 44
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgag gattatatga tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcattt attaatctgc ctggtggtcg tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacagact 300

catgggctga ctggttattt tgactactgg ggtcagggaa ccctggtcac cgtctcgagc 360

<210> 45
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 45
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt ttgtatggta tggcttgggc ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatcg attgggatgc atggtgatac tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaagtttgt 300

ggggctacgt attgtaattt tgactactgg ggtcagggaa ccctggtcac cgtctcgagc 360

<210> 46
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 46
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt aagtatgtta tggcttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaatt attgattcct tgggttctac tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaagggggt 300

ttgttggttc attatgattt tgactactgg ggtcagggaa ccctggtcac cgtctcgagc 360

<210> 47
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 47
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgag gtgtatggta tgtcttgggc ccgccaggct 120

ccagggaagg gtctagagtg ggtctcattg attgatgcgg gtggtcggaa tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaatcgacg 300

acgcgtgctt atagtgatta ttttgactac tggggtcagg gaaccctggt caccgtctcg 360

agc 363

<210> 48
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 48
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgag aattatgata tgcattgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaggg attactacgc atggtaggcg tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaaagtgat 300

aatttgaata tgaatgtgga ttttgactac tggggtcagg gaaccctggt caccgtctcg 360

agc 363

<210> 49
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 49
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttatt aagtatgata tgtgttgggc ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatgt attgagtcta gtggtcagaa tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaatgtctg 300

aatgatagtt gtaatgttca ttttgactac tggggtcagg gaaccctggt caccgtctcg 360

agc 363

<210> 50
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 50
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggGtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggt aattataata tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcagat attggtcgtt atggtagggt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggat accgcggtat attactgtgc gaaaactcag 300

cgtatggtta atccgtcgcc ttttgactac tggggtcagg gaaccctggt caccgtctcg 360

agc 363

<210> 51
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 51
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggGtc cctgcgtctc 60

tcctgtgcag cttccggatt cacctttgtt agttatagta tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaatt atttcggggc agggtactgt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaatcgccg 300

atggtttttg ctttggatgg gaggtctttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 52
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 52
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtacag cctccggatt caccttttct gagtatagta tggggtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaagt attacgcctg ttggtgtttt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaagggagg 300

cctgggccgc atggttggtc ttttcggttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 53
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 53
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttggg cagtatatga tgggttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcaact attgataagt cgggttatag tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaaagtggg 300

attgattcgc ggggtctgat gactaagttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 54
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 54
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt cacctttgct cgttatcgta tggcgtgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatct attctgagtg atggtgcggt tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaacctggg 300

gggaatgcgt ggtctactcg ggttactttt gactactggg gtcagggaac cctggtcacc 360

gtctcgagc 369

<210> 55
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> modified_base
<222> (99)..(99)
<223> a, c, g, t, unknown or other

<400> 55
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt caccttttt acgtatacna tggcttgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatct attacgccgc ttggttataa tacatactac 180

gcagactccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaaccgtcg 300

gatgtgaagg tgtctccgct gccgagtttt gactactggg gtcggggaac cctggtcacc 360

gtctcgagc 369

<210> 56
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 56
gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgcgtctc 60

tcctgtgcag cctccggatt caccttact atgtatggta tgcattgggt ccgccaggct 120

ccagggaagg gtctagagtg ggtctcatcg atttctcagt atggtctttc tacatactac 180

gcagattccg tgaagggccg gttcaccatc tcccgcgaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgcg tgccgaggac accgcggtat attactgtgc gaaagggtct 300

atgaggcggg tgtttagtag ttcggatact tttgactact ggggtcaggg aaccctggtc 360

accgtctcga gc 372

<210> 57
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 57
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga ccgtgtcacc 60

atcacttgcc gggcaagtca gaatataggt gatcggttac attggtacca gcagaaacca 120

gggaaagccc ctaagctcct gatctatcgt atttcccgtt tgcaaagtgg ggtcccatca 180

cgtttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg ctacgtacta ctgtcaacag tttgggctgt atcctactac gttcggccaa 300

gggaccaagg tggaaatcaa acgg 324

<210> 58
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 58
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 59
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 59
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 60
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 60
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 61
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 61
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 62
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 62
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 63
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 63
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly His Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Ser Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Arg Ala Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 64
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 64
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 65
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 65
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 66
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 66
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr His Ser Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Arg Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 67
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 67
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln His Ile Asn Ala Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Gln Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Val Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 68
<211> 108
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 68
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Ala Thr Asn Pro Ala
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 69
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 69
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Gln Ala Ser Phe Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 70
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 70
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 71
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 71
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Arg Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 72
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 72
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ala
        35   40   45

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 73
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 73
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Met Arg Pro Met
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Trp
100 105

<210> 74
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 74
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 75
<211> 108
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 75
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser His Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Met Ser Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 76
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 76
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser His Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Met Thr Ala Pro Phe

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                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 77
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 77
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Tyr Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Val Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Gln Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 78
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 78
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Gly His Gly
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
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Tyr Trp Val Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Leu Ser Lys Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 79
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 79
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Asn Ile His Asn Arg
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Arg Gln Trp Ile Gln Pro Pro Trp
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 80
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 80
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr His Ser Ser Gly Leu Gln Ser Gly Val Pro Leu Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 81
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 81
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 82
<211> 108

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 82
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
20 25 30

Leu Gly Trp Tyr Leu Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 83
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 83
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 84
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 84
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
            20                  25                  30


Ile Ser Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Arg Ala Ser Tyr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Gly Ile Lys Arg
            100                 105


<210> 85
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 85
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
            20                  25                  30


Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

Tyr Arg Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Tyr Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 86
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 86
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
            20   25   30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Arg Ala Ser Asn Met Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 87
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 87

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
            20                  25                  30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Val
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 88
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 88
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
            20                  25                  30

Ile Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Arg Gly Trp Gly Arg Pro Val
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 89
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<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 89
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Ile Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Glu Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Lys Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 90
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 90
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Met Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 91
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 91
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Ser Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 92
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 92
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Lys Leu Leu Ile

35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Glu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 93
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 93
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Leu Trp Tyr Gln Leu Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Ala Gln Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 94
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 94
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
            20   25   30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Ala
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 95
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 95
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 96
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 96
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Leu Ser Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ala Leu Asn Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 97
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 97
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Lys Ile Gly Thr Gly
20 25 30

Leu Arg Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Val Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Phe Pro Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 98
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 98
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Thr Gly
20 25 30

Leu Arg Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Met Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Trp Tyr Arg Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 99
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 99
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Gly His Met
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Trp Phe Gly Ser Val Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Val Gln Gly Arg Leu Arg Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 100
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 100
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Asn His Trp
20 25 30

Leu Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Thr Leu Leu Ile
35 40 45

Ser Gly Val Ser Trp Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Cys Gln Pro Gly Phe Arg Pro Cys
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 101
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 101
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Gln
            20   25   30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Arg Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Ser Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 102
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 102
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Gly Ala
            20   25   30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Arg Ala Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Ala Leu Val Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 103
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 103
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Arg
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asn Ala Ser Phe Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Ser Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 104
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 104
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Arg
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gln Ser Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Val Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 105
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 105
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ala Ser Met Pro Ile
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 106
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 106
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Gly His Met
20 25 30

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Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Arg Ala Ala Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 107
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 107
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 108
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 108
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Thr Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 109
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 109
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Phe
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 110
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 110
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly His Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 111
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 111
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Ile Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 112
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 112
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Trp Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 113
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 113
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

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Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Val Leu Leu His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 114
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 114
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Leu Leu Leu Asp Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 115
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
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<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 115
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ala Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Glu Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ser Ser Val Leu Ile Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 116
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 116
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg

100 105

<210> 117
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 117
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 118
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 118
Asp Ile Gln Met Thr Gln Ser Ser Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

```
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Ala Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 119
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 119
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Arg Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30


Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 120
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 120
Asp Thr Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Gly His Ser
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            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 121
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 121
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Val Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 122
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 122
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 123
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 123
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 124
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 124
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 125
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 125
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 126
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 126
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 127
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 127
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20   25   30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85   90   95

Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 128
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 128
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20   25   30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85   90   95

Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 129
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 129
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 130
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 130
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 131
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 131
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Arg Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 132
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 132
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

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    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 133
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 133
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Phe Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 134
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 134
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
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```
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Phe Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 135
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 135

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 136
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 136
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Asn Lys Arg
100 105

<210> 137
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 137
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Phe Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Arg
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 138
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 138
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 139
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 139
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

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Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95


Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 140
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 140
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30


Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Trp Gly Ser Asp Leu Tyr Lys Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95


Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 141
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 141
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
```

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Thr Pro Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 142
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 142
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 143
<211> 108
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 143
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Ile Ser His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 144
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 144
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ala Ile Asp His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe

```
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 145
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 145
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 146
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 146
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Thr
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

```
Tyr Trp Ala Ser Asp Leu Ile Arg Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 147
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 147

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ala
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 148
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 148

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ala Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 149
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 149
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Asp Leu Ser Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 150
<211> 108

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 150
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 151
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 151
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Thr Ile Gly His Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95


Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 152
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 152
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30


Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Met Arg Thr Pro Phe
                85                  90                  95


Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 153
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 153
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Arg Ile Gly Ser Ser
            20                  25                  30


Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85   90   95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 154
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 154
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Gly His Ser
            20   25   30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85   90   95

Met Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 155
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 155

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly His Ser
            20                  25                  30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Ala Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Arg Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 156
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 156
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 157
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<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 157
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Arg Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ile Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 158
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 158
Asp Leu Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Ser Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 159
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 159
Asp Phe Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Gly Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 160
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 160
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val

```
        35                  40                  45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 161
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 161
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Glu Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
                85                  90                  95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 162
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 162
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Glu Ser Ile Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Leu Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 163
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 163
Asp Ile Gln Met Ile Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Glu Arg Val Thr Ile Ile Cys Gln Ala Ser Gln Arg Ile Gly Ser Asn
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Ser Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 164
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 164
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 165
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 165
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Glu Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 166
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 166
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ser Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Glu Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 167
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 167
Asp Leu Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Tyr Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 168
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 168
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Ala Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Arg Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe
85 90 95

Ala Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 169
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 169
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Glu Ile Asp His Gly
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Val Ala Ala Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 170
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 170
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Leu Asn
            20   25   30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Thr Leu Leu Ile
        35   40   45

Tyr Trp Ser Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Arg Met Arg Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 171
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 171
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly His Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Ser Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Arg Ala Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 172
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 172
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Lys Gly
20 25 30

Leu Met Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Glu Val Glu Ile Lys Arg
100 105

<210> 173
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 173
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 174
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 174
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Gln Ser
20 25 30

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Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Ala Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Met Arg Arg Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 175
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 175
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Lys Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Val Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Val Ser Arg Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 176
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 176
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ala Ile Ser Asn Gly
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Thr Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Leu Arg Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 177
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 177
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ala Asn Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Val Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ile Ala Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 178
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 178
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Thr Ile Gly His Gly
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ser Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 179
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 179
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Asn Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser Tyr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Arg Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 180
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 180
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 181
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 181
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 182
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 182
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 183
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 183
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Leu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 184
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 184
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Glu Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Val Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg

100 105

<210> 185
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 185
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 186
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 186
Asp Ile Gln Met Thr Gln Ser Pro Thr Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 187
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 187
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Arg Gly Lys Ala Pro Glu Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 188
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 188
Asp Ile Gln Ile Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala

20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Glu Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Val Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 189
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 189
Asp Ile Gln Ile Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Phe Thr Cys Gln Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Leu
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 190
<211> 108
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 190
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Glu Arg
100 105

<210> 191
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 191
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Asn Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Leu Pro
65 70 75 80

Glu Asp Tyr Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 192
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 192
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Gly Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Phe Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 193
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 193
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Ala Ser
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Ser Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Gly Met Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 194
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 194
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Gly His Met
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Trp Phe Gly Ser Val Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Val Gln Gly Arg Leu Arg Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 195
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 195
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Gly His Gln
            20   25   30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Ala Trp Ser Ser Val Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Arg Gln Asp Leu Ser Leu Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 196
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 196
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Ala Thr Asn Pro Ala
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 197
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 197
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Ala Leu Asp
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Lys Gly Trp Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ala Gln Gly Trp Gly Arg Pro Val
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 198
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 198
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 199
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 199
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 200
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 200
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly

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    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 201
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 201
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
            20                  25                  30

Ile Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 202
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 202
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Ser Ser Ile Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 203
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 203
Asp Ile Leu Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
            20   25   30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Ser Ser Ile Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 204
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 204
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Arg
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gln Ser Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Val Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 205
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 205
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 206
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 206
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr His Ser Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 207
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 207
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Leu Ser Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ala Leu Asn Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 208
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 208
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Leu Asn
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ser Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Arg Met Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 209
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 209
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

```
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Tyr Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Trp Val Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Gln Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105


<210> 210
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 210
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Ser Ala
            20                  25                  30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Arg Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Ile Arg Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105


<210> 211
<211> 108
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 211
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Gly Ala
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Val Ala Leu Val Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 212
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 212
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Arg Ile Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Arg Ser Ala Pro Phe

```
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105


<210> 213
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 213
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105


<210> 214
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 214
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
            20                  25                  30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
        35                  40                  45
```

```
Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105
```

<210> 215
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 215

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr His Ser Ser Gly Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Arg Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
            100                 105
```

<210> 216
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 216

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
```

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Leu Asn
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ser Ser Met Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Arg Met Arg Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 217
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 217
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
20 25 30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 218
<211> 108

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 218
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Arg
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Gln Ser Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Val Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Cys
100 105

<210> 219
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 219
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Tyr Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Val Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Gln Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 220
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 220
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ser Val
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Ser Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Leu Arg Ser Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 221
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 221
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Arg
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Gln Ser Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Thr Ala Leu Val Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 222
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 222
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Gly Ala Ser
            20   25   30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
        35   40   45

Tyr Trp Gly Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln Ser Leu Arg Thr Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 223
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 223

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Thr Ile Gly His Gly
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ser Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Leu Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 224
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 224
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ala
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Arg Ser His Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ile Ala Leu Thr Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 225

<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 225
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln His Ile Asn Ala Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Asp Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Gln Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Val Arg Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 226
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 226
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln His Ile Asn Ala Ser
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Gln Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Val Arg Thr Pro Phe
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 227
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 227

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Ala Thr Asn Pro Ala
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 228
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 228

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
```

```
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 229
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 229
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 230
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 230
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 231
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 231
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 232
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 232
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 233
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 233
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Thr Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 234
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 234
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 235
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 235
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 236
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 236
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Gln Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 237
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 237
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Arg Glu Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 238
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 238
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Ser Ser Arg Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 239
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 239
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Tyr Leu Arg Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 240
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 240
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 241
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 241
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 242
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 242
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

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Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Arg Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Arg Val Glu Ile Lys Arg
            100                 105


<210> 243
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 243
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Ala Ser Arg Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 244
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 244
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Arg Arg
100 105

<210> 245
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 245
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Lys Leu Thr Arg Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Asn Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 246
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 246
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 247
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 247
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 248
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 248
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 249
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 249
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

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Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Ala Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 250
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 250
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Ser Ser Met Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 251
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
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<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 251
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 252
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 252
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg

100 105

<210> 253
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 253
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Gln Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 254
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 254
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 255
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 255
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 256
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 256
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe

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            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Met Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 257
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 257
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 258
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 258
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 259
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 259
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 260
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 260
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Gln Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 261
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 261
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 262
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 262
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 263
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 263
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 264
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 264
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 265
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 265
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Ala Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 266
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 266
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Arg Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Arg Val Glu Ile Lys Arg
100 105

<210> 267
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 267
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 268
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 268
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly

```
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ser Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 269
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 269
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 270
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 270
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 271
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 271
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Tyr Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Thr Asn Pro Ala
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 272
<211> 120
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 272
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 273
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 273
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 274
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 274
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Thr Tyr
20 25 30

Lys Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr Arg Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 275
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 275

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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Leu Tyr
            20                  25                  30


Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Arg Lys Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 276
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 276
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30


Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Asp Asp Thr Gly Thr Gln Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
```

100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 277
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 277
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Trp Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Asp Ser Leu Gly Leu Gln Ala Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Met Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Tyr Ser Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 278
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 278
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu His Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Arg Tyr
20 25 30

```
His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Val Ile Asp Ser Leu Gly Leu Gln Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Glu Tyr Gly Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115


<210> 279
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 279
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
            20                  25                  30

His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Val Ile Asp Ser Leu Gly Leu Gln Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Glu Tyr Ser Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115
```

<210> 280
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 280
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Asp Ser Leu Gly Leu Gln Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Tyr Gly Gly Ala Phe Asp Tyr Trp Gly Pro Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 281
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 281
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Asp Tyr
20 25 30

Asp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser His Ile Asp Arg Gly Gly Thr Leu Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Thr Leu Met Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 282
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 282
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala His Tyr
20 25 30

His Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Pro Ala Asp Gly Leu Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Glu Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 283
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 283
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Thr Tyr
20 25 30

Lys Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr Arg Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 284
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 284
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Thr Tyr
20 25 30

Thr Met Arg Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Asn Ser Ser Gly Thr Leu Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

```
                85                  90                  95

Ala Lys Ser Ser Ser Tyr Thr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> 285
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 285
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Trp Phe Tyr
            20                  25                  30

Asp Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Thr His Asn Gly Lys Thr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Gly Gln Leu Thr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> 286
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 286
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Leu Tyr
            20                  25                  30

Gln Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Met Pro Ser Gly Asn Leu Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Met Trp Ser Leu Asn Leu Gly Phe His Ala Ala Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 287
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 287
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Leu Tyr
            20                  25                  30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Lys Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
            100                 105                 110
```

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 288
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 288
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Leu Tyr
            20   25   30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Met Ser Asn Gly Thr Arg Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Arg Glu Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 289
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 289
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Leu Tyr
            20   25   30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Arg Glu Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 290
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 290
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Val Ser
20 25 30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 291
<211> 121
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 291
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Thr Ala
20 25 30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 292
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 292
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Gly Tyr
20 25 30

Thr Met Glu Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Thr Pro Leu Gly Ala Asn Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Ile Arg Tyr Thr Gly Thr Tyr Asn Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 293
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 293
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Thr Tyr
20 25 30

Ala Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Phe Ile Pro Gly Ala Gly Gly Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ala Val Asp Gly Leu Ala Asn Ala Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 294
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 294
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ala Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Glu Ile Ser Pro Tyr Gly Asn His Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Pro Asp Arg Arg Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100   105   110

Thr Val Ser Ser
        115

<210> 295
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 295
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe His Ser Tyr
            20   25   30

His Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Asp Ala His Gly Phe Thr Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Arg Gly Gly Pro Leu Ser Thr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 296
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 296
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Thr Glu
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Tyr Val Pro Gly Ser Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Arg His Ser Asp Val Glu Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 297
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 297
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

```
Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Asp Asp Thr Gly Thr Gln Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 298
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 298
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Phe Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 299
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 299
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 300
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 300
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe His Arg Trp
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 301
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 301
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg His
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 302
<211> 120
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 302
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Lys Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 303
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 303
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Val Arg Gln
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 304
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 304
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Ser
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 305
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 305
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Leu His
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 306
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 306
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Ala Ser
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 307
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 307
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Ser Ser
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 308
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 308
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Lys Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 309
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 309
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Thr Ser
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 310
<211> 120
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<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 310
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 311
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 311
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

```
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 312
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 312
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
            20                  25                  30


Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 313
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 313
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
            20   25   30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Ile Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 314
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 314
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

```
Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 315
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 315
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
            20                  25                  30


Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 316
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 316
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Val Lys Ala
```

```
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 317
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 317
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gln His Ser
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 318
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 318
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Glu Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 319
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 319
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Arg Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 320
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 320
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Ser
20 25 30

Asn Met Ser Trp Gly Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 321
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 321
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Lys Ser
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 322
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 322
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Leu Ser
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 323
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 323
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Arg Ser
            20                  25                  30


Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 324
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 324
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Arg Ser
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 325
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 325
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gln Arg Ser
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 326
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 326
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Tyr Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 327
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 327
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser His Asn
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 328
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 328
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Leu Gln
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 329

<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 329
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 330
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 330
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn His Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Tyr Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 331
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 331
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe His Arg Ala
            20                  25                  30


Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Ser Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 332
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 332
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Arg Thr
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 333
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 333
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ser Ile Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 334
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 334
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 335
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 335
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Leu Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Ser Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 336
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 336
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Arg Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Gly Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 337
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 337
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ala Gly Pro Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asp Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 338
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 338
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asn Gly Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 339
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 339
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Lys Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Arg
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 340
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 340
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 341
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 341
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 342
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 342
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30


Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Asn Asn Gly Pro Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 343
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 343
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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Gly Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 344
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 344

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ser Ser Gly Pro Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
```

100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 345
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 345
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Phe Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 346
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 346
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

```
Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Ser Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 347
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 347
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Gln Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Ser Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 348
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 348
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Ile Gly Ile Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 349
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 349
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Ile Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 350
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 350
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Thr Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 351
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 351
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Glu Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 352
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 352
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ser Ser Gly Tyr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

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                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 353
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 353
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Asp Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Ser Gly Ile Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 354
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 354
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ser Ser Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 355
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 355
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ser Arg Gly Pro Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 356
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 356
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Ile Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 357
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 357
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Asp Gly Gly Leu Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 358
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 358
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ser His Gly Gly Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 359
<211> 120
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 359
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Gly Ser Gly Gln Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 360
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 360
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Asn Gly Pro Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 361
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 361
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 362
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 362
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Lys Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 363
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 363
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Lys Ser
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 364
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 364
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Lys Ser
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 365
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 365
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Arg Ser
20 25 30

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Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 366
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 366
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Arg Ser
            20                  25                  30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
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<210> 367
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 367
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 368
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 368
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 369
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 369
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Lys Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 370
<211> 120
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 370
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Asp Lys
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 371
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 371
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 372
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 372
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Val Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 373
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 373
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro His Ser
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 374
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 374
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Ile Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110
```

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 375
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 375
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Asp Asp Thr Gly Thr Gln Thr Phe Tyr Glu Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 376
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 376
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45

Ser Trp Ile Asp Asp Ile Gly Ser Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 377
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 377
Glu Val Gln Leu Trp Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Asp Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 378
<211> 120
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<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 378
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 379
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 379
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Asp Asp Ile Gly Ser Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 380
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 380
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Ser Tyr
            20                  25                  30


Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Thr Ile Ala Asp Thr Gly Gly Leu Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Ala Tyr Val Leu Asp Asp Gln Pro Ala Phe Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 381
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 381
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Val
            20   25   30

Ser Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Gly Ile Asp Gly Pro Gly Ser Asn Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Asn His Ala Gly Ser Thr Arg Asn Val Phe Asp Tyr Trp Ser
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 382
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 382
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Ser Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Arg Pro Ser Gly Leu Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

```
Ala Lys Gln Arg Ala Arg Arg Tyr Gln Asp Arg Pro Arg Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 383
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 383
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ala Gly Phe Thr Phe Asp His Thr
            20                  25                  30


Glu Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ala Ile Thr Ser Asp Gly Leu Asn Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Gln Asp Arg Pro Pro Trp Ser Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 384
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 384
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Asp Ser Gly Leu Thr Phe Ser Ser Tyr
```

20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Thr Asp Gly Met Gly Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Leu Ser Ala Pro Val Leu Met Ala Tyr Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 385
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 385
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Pro Tyr
20 25 30

Thr Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Ser Ser Ser Gly Arg Lys Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Phe Arg Lys Ser Ser Val Leu Arg Ser Met Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 386
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 386
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Gly Gly Leu Gly Lys Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Ser Asn Met Tyr Arg Ser Ile Lys Tyr Pro Phe Ala Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 387
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 387
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Lys Tyr
20 25 30

Gly Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Asn Gly Ser Gly Ile Trp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly His Val His Ser Pro Pro Arg Gly Pro Phe Leu Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 388
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 388
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Ser Tyr
20 25 30

Ser Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Met Pro Ser Gly Gln Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asn Gln Ser His Gln Arg Arg Gly Ile Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 389
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 389
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Glu Tyr
20 25 30

Ser Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser His Ile Ser Arg Asp Gly Glu Phe Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Asn Ala Asp Leu Gly Trp Val Gln Pro His Leu Phe Val
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 390
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 390
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Trp Arg Tyr
20 25 30

Asn Met Gly Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Pro Thr Gly Ser Ile Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Trp Ile Gly Leu Met Ser Leu His Pro Ala Asp Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 391
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 391
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Thr Glu
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Tyr Val Pro Gly Ser Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Arg His Ser Asp Val Glu Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110


Thr Leu Val Thr Val Ser Ser
        115


<210> 392
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 392
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
```

```
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Asp Arg
            20                  25                  30

Cys Met Met Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Gln Val Glu Gly Asn His Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Cys Met Thr Val Gly Pro Gly Asn Ser Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 393
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 393
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Thr Tyr
            20                  25                  30

Lys Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr Trp Gly
            100                 105                 110
```

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 394
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 394
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Gly Thr Tyr
            20   25   30

Lys Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Ile Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr Trp Gly
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 395
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 395
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

```
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Asp Asp Thr Gly Thr Gln Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 396
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 396
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Thr Tyr
            20                  25                  30

Lys Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Cys
        115                 120


<210> 397
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<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 397
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln His Ile Asn Ala Ser
            20   25   30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr Trp Ala Ser Gln Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Met Val Arg Thr Pro Phe
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 398
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 398
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Tyr Lys Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 399
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 399
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Ile Ser Asp Glu
            20                  25                  30


Asp Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Tyr Gly Pro Ser Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Ser Ala Leu Glu Pro Leu Ser Glu Pro Leu Gly Phe Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 400
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 400
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
```

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Asn
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 401
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 401
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Asp Ser Leu Gly Leu Gln Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Tyr Gly Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 402
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 402
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Ala Tyr
20 25 30

Ser Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Pro Leu Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Gln Thr Ala Tyr Leu Asn Arg Ala Thr Glu His Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 403
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 403
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ala Tyr
20 25 30

Ser Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Thr Pro Gln Gly Asp Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Gln Ala Gly Trp Ser Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 404
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 404
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Val Asp Tyr
20 25 30

Glu Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Asn Asp Gly Ala Ala Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Asp Ala Ala Phe Asp Tyr Trp Gly Gln Gly Ala Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 405
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 405
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Ala Tyr
20 25 30

Ser Met Gly Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Thr Gly Asn Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ala Glu Glu Pro Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 406
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 406
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
20 25 30

His Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Asp Ser Leu Gly Leu Gln Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Glu Tyr Gly Gly Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 407
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 407
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr His Tyr
            20                  25                  30


Ser Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser His Ile Thr Pro Asp Gly Leu Ile Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Gly Arg Leu Val Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110


Val Thr Val Ser Ser
        115


<210> 408
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 408
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
```

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Asn Tyr
20 25 30

Gly Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Asn Ile Gly Arg Ala Gly Ser Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gln Ser Trp Arg Thr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 409
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 409
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Ala Tyr
20 25 30

Ser Met Gly Trp Val Arg Gln Ala Pro Glu Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Asp Gly Arg Gly Ala Glu Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ile Asp Thr Leu Ile Ser Glu Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
        115

<210> 410
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 410
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Asn Tyr
            20   25   30

Thr Met Trp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Ser Gly Thr Gly His Thr Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Phe Gly Pro Asn Asn Pro Met Phe Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Leu Val Thr Val Ser Ser
        115

<210> 411
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 411
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Ser Tyr
            20   25   30

```
Asp Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Ser Ala Asp Gly Thr Phe Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Ser Phe Asp Lys Tyr Asn Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115


<210> 412
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 412
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Lys Tyr
            20                  25                  30

Thr Met Trp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Asp Pro Val Gly Asn Leu Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Gly Pro Thr Ser Ser Asn Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115


<210> 413
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<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 413
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Glu Tyr
20 25 30

Gly Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Asp Asn Val Gly Ser Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Thr Thr Pro Val Leu Leu Pro Leu Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 414
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 414
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Tyr
20 25 30

Asn Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ala Ala Asn Gly Arg Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

```
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Met Thr Asn Met Ala Tyr Gly Ser Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 415
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 415
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Leu Tyr
            20                  25                  30


Ser Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser His Ile Asp Arg Ala Gly Met Ile Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Ser Asn Ala Val Asn Met Gln Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 416
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 416
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Lys Tyr
20 25 30

Thr Met Trp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Asp Pro Val Gly Asn Leu Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Arg His Arg Pro Ser Thr Gln Asp Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 417
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 417
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Asp Tyr
20 25 30

Lys Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Asp Lys Gly Gly Ile Ile Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Lys Met Phe Pro Lys Phe Arg Pro Ala Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 418
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 418
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Asp Tyr
            20                  25                  30


Gly Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser His Ile Asn Arg Ser Gly Leu Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Val Leu Asn Ala Pro Asn Phe Lys Phe Asp Tyr Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 419
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 419
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
            20                  25                  30

Ala Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Asp Gly Asn Gly Leu Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Arg Thr Arg Ser His Ser Asp Ser Gly Trp Ala Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 420
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 420
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asn Tyr
            20                  25                  30

Asn Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Thr Lys Gly Gly Arg Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Leu Gly Pro Ser Arg Met Leu Asn Glu Pro Leu Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
```

115 120

<210> 421
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 421
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Pro Ala Tyr
20 25 30

Ser Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Ser Pro Leu Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Gln Thr Ala Tyr Leu Asn Arg Ala Thr Glu His Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 422
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 422
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Lys Tyr
20 25 30

Asp Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Tyr Ala Ile Gly Gly Asn Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Leu Lys Ser Gly Met Gln Thr Arg Leu Asn Ser Phe Asp Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 423
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 423
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Leu Tyr
            20   25   30

Gln Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Thr Ile Met Pro Ser Gly Asn Leu Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Met Trp Ser Leu Asn Leu Gly Phe His Ala Ala Phe Asp Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 424
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 424
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Gln Tyr
20 25 30

Gly Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Pro Ser Gly Asn Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Asn Gly Ser Leu Pro Pro Arg Gly Ser Ile Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 425
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 425
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asn Tyr
20 25 30

Asn Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Thr Lys Gly Gly Arg Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Leu Gly Pro Ser Arg Met Leu Asn Glu Pro Leu Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 426
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 426
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Thr Tyr
            20                  25                  30


Tyr Met Gly Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Gly Ala Asn Gly Ala Pro Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Ile Arg Ser Leu Asn Arg Trp Ala Glu Pro Val Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 427
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 427
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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Asp Tyr
            20                  25                  30

Ser Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gln Ile Ser Pro Ala Gly Ser Phe Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Asp Ser Lys Ser Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115


<210> 428
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 428
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Lys Thr Tyr
            20                  25                  30

Thr Met Arg Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Asn Ser Ser Gly Thr Leu Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Ser Ser Tyr Thr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
```

100 105 110

Val Thr Val Ser Ser
115

<210> 429
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 429
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Met Tyr
20 25 30

Ser Met Lys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Asn Ala Gly Asp Ile Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Glu Ser Phe Arg Ser Arg Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 430
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 430
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

```
Leu Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Leu Ile Arg Met Arg Gly Ser Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys His Ser Leu Thr Thr Asn Leu Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115


<210> 431
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 431
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Asp Tyr
            20                  25                  30

Met Met Ala Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ile Ile Gly Thr Thr Gly Thr Trp Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Thr Asn Ala Tyr Glu Ser Glu Phe Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser
        115
```

<210> 432
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 432
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Arg Tyr
20 25 30

Thr Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile His Phe Asp Gly Arg Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asn Glu Trp Ala Ser Leu Lys His Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 433
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 433
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Asp Tyr
20 25 30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Phe Ile Asn Leu Pro Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Thr His Gly Leu Thr Gly Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 434
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 434
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Leu Tyr
20 25 30

Gly Met Ala Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Gly Met His Gly Asp Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Cys Gly Ala Thr Tyr Cys Asn Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 435
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 435
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Lys Tyr
20 25 30

Val Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ile Ile Asp Ser Leu Gly Ser Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Gly Leu Leu Val His Tyr Asp Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 436
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 436
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Val Tyr
20 25 30

Gly Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Asp Ala Gly Gly Arg Asn Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

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                85                  90                  95

Ala Lys Ser Thr Thr Arg Ala Tyr Ser Asp Tyr Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 437
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 437
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Glu Asn Tyr
            20                  25                  30

Asp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Gly Ile Thr Thr His Gly Arg Arg Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Ser Asp Asn Leu Asn Met Asn Val Asp Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 438
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 438
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ile Lys Tyr
            20                  25                  30

Asp Met Cys Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Cys Ile Glu Ser Ser Gly Gln Asn Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Cys Leu Asn Asp Ser Cys Asn Val His Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 439
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 439
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asn Tyr
            20                  25                  30

Asn Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Asp Ile Gly Arg Tyr Gly Arg Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Thr Gln Arg Met Val Asn Pro Ser Pro Phe Asp Tyr Trp Gly
            100                 105                 110
```

Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 440
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 440
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Val Ser Tyr
            20   25   30

Ser Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ile Ile Ser Gly Gln Gly Thr Val Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Pro Met Val Phe Ala Leu Asp Gly Arg Ser Phe Asp Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 441
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 441
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Glu Tyr
            20   25   30

Ser Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ser Ile Thr Pro Val Gly Val Phe Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Gly Arg Pro Gly Pro His Gly Trp Ser Phe Arg Phe Asp Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 442
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 442
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Gln Tyr
            20   25   30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Thr Ile Asp Lys Ser Gly Tyr Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Gly Ile Asp Ser Arg Gly Leu Met Thr Lys Phe Asp Tyr
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 443
<211> 123
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 443
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ala Arg Tyr
20 25 30

Arg Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Leu Ser Asp Gly Ala Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Pro Gly Gly Asn Ala Trp Ser Thr Arg Val Thr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 444
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 444
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Met Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Gln Tyr Gly Leu Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Ser Met Arg Arg Val Phe Ser Ser Ser Asp Thr Phe Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 445
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 445
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Tyr
20 25 30

Asp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gln Ile Ser Ala Asp Gly His Phe Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Arg Ser Ser Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 446
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 446
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
            20   25   30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Arg Ile Asp Ser His Gly Asn Arg Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys His Met Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100   105   110

Thr Val Ser Ser
        115

<210> 447
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 447
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Glu Tyr
            20   25   30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Arg Ile Asn Gly Val Gly Asn Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

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Ala Lys His Gln Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 448
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 448
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20                  25                  30


Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Arg Ile Thr Ser Glu Gly Ser His Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys His Thr Ser Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 449
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 449
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Arg Tyr
            20                  25                  30
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```
Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Arg Ile Ser Gly Pro Gly Thr Val Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys His Asp Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115


<210> 450
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 450
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30

Ala Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Glu Ile Ser Pro Tyr Gly Asn His Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Pro Asp Arg Arg Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser
        115
```

<210> 451
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 451
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Ser Tyr
20 25 30

Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Thr Asp Gly Met Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Gly Val Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 452
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 452
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Tyr
20 25 30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ile Ile Arg Val Pro Gly Ser Thr Thr Tyr Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Lys Gly Asp Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 453
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 453
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ile Leu Tyr
20 25 30

Asp Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Arg Ile Ser Ala Asn Gly His Asp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Pro His Tyr Leu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 454
<211> 117
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 454
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Lys Tyr
20 25 30

Phe Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Leu Ile Asp Pro Arg Gly Pro His Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Leu Gly Glu Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 455
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 455
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
35 40 45

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 456
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 456
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser His Ser
            20                  25                  30


Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Met Thr Thr Pro Phe
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 457
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 457
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Ile Gly Thr Ser
            20                  25                  30


Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Thr
        35                  40                  45
```

Tyr Gln Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Ala Leu Arg Pro Met
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 458
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 458
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Thr Gly
            20   25   30

Leu Arg Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Met Leu Leu Ile
        35   40   45

Tyr Arg Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Thr Thr Leu Gln Pro Phe
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 459
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 459

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser His Ser
20 25 30

Leu Val Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Leu Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Met Thr Thr Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 460
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 460
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Gly Asp Arg
20 25 30

Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ile Ser Arg Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Gly Leu Tyr Pro Thr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 461

<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 461
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Tyr
            20   25   30

Asp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Gln Ile Ser Ala Asp Gly His Phe Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Lys Ser Arg Ser Ser Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100   105   110

Thr Val Ser Ser
        115

<210> 462
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 462
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
            20   25   30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Arg Ile Asp Ser His Gly Asn Arg Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys His Met Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 463
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 463
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Glu Tyr
            20                  25                  30


Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Arg Ile Asn Gly Val Gly Asn Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys His Gln Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 464
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 464
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Arg Ile Thr Ser Glu Gly Ser His Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys His Thr Ser Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 465
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 465
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Arg Tyr
20 25 30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Arg Ile Ser Gly Pro Gly Thr Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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Ala Lys His Asp Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 466
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 466
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30


Ala Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Glu Ile Ser Pro Tyr Gly Asn His Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Lys Pro Asp Arg Arg Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110


Thr Val Ser Ser
        115


<210> 467
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 467
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Ser Tyr
20 25 30

Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Thr Asp Gly Met Val Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Gly Val Asn Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 468
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 468
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Asp Tyr
20 25 30

Met Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ile Ile Arg Val Pro Gly Ser Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gln Lys Gly Asp Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser

115

<210> 469
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 469
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ile Leu Tyr
20 25 30

Asp Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Arg Ile Ser Ala Asn Gly His Asp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Gly Pro His Tyr Leu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 470
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 470
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Lys Tyr
20 25 30

Phe Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Leu Ile Asp Pro Arg Gly Pro His Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Gln Leu Gly Glu Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115
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<210> 471
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> MOD_RES
<222> (33)..(33)
<223> Any amino acid

<400> 471

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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Phe Thr Tyr
            20                  25                  30

Xaa Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ser Ile Thr Pro Leu Gly Tyr Asn Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Lys Pro Ser Asp Val Lys Val Ser Pro Leu Pro Ser Phe Asp Tyr
            100                 105                 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120
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<210> 472
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 472
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
1 5 10 15

Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe Leu
20 25 30

Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala Thr
85 90 95

Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 473
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 473
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 474
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 474
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Gln Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 475
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 475
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Arg Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 476
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 476
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 477
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 477
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 478
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 478
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg

100 105

<210> 479
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 479
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Tyr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 480
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 480
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg Gln Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 481
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 481
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Arg Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 482
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 482
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe

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            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 483
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 483
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Gln Met Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 484
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
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<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 484
Arg Ala Ser Arg Pro Ile Trp Pro Phe Leu Glu
1 5 10

<210> 485
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 485
Phe Thr Ser Arg Leu Gln Ser
1 5

<210> 486
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 486
Leu Gln Asn Val Ser Met Pro Ala Thr
1 5

<210> 487
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 487
Arg Ala Ser Gln Tyr Ile Gly Ser Ala Leu Ser
1 5 10

<210> 488
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 488
Arg Ala Ser Asn Leu Gln Ser
1 5

<210> 489
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 489
Gln Gln Leu Ala Ile Arg Pro Phe Thr
1 5

<210> 490
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 490
Arg Ala Ser Arg Asp Ile Ala Leu Asp Leu Leu
1 5 10

<210> 491
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 491
Gly Trp Ser Gly Leu Gln Ser
1 5

<210> 492
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 492
Ala Gln Gly Trp Gly Arg Pro Val Thr Phe Gly Gln Gly Thr Lys Val
1 5 10 15

Glu Ile Lys Arg
20

<210> 493
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 493
Arg Ala Ser Gln Pro Ile Gly His Ser Leu Ala
1 5 10

<210> 494
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 494
Trp Ala Ser Thr Leu Gln Ser
1 5

<210> 495
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 495
Gln Gln Met Leu Arg Thr Pro Phe Thr
1 5

<210> 496
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 496
Arg Ala Ser Gln Arg Ile Gly Ser Asn Leu Ala
1 5 10

<210> 497
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 497

Trp Ala Ser Leu Leu Gln Ser
1   5

<210> 498
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 498
Gln Gln Thr Arg Ser Ala Pro Phe Thr
1   5

<210> 499
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 499
Arg Ala Ser Gln Ser Ile Gly His Ser Leu Val
1   5   10

<210> 500
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 500
Trp Ala Ser Leu Leu Gln Ser
1   5

<210> 501
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 501
Gln Gln Ser Arg Ala Ala Pro Phe Thr Phe Gly Gln Gly Thr Lys Val
1   5   10   15

Glu Ile Lys Arg
            20

<210> 502
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 502
Arg Ala Ser Gln Tyr Ile Gly Thr Ala Leu Asn
1 5 10

<210> 503
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 503
Arg Arg Ser His Leu Gln Ser
1 5

<210> 504
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 504
Gln Gln Ile Ala Leu Thr Pro Tyr Thr
1 5

<210> 505
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 505
Arg Ala Ser Gln Pro Ile Gly Ser Val Leu Ala
1 5 10

<210> 506
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 506
Phe Ser Ser Ile Leu Gln Ser
1 5

<210> 507
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 507
Gln Gln Ala Leu Arg Ser Pro Phe Thr
1 5

<210> 508
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 508
Arg Ala Ser Gln Tyr Ile Gly Thr Ser Leu Ala
1 5 10

<210> 509
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 509
His Ser Ser Gly Leu Gln Ser
1 5

<210> 510
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 510
Gln Gln Thr Ala Leu Arg Pro Phe Thr
1 5

<210> 511

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 511
Arg Ala Ser Gln His Ile Asn Ala Ser Leu Gly
1   5   10

<210> 512
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 512
Trp Ala Ser Gln Leu Gln Ser
1   5

<210> 513
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 513
Gln Gln Met Val Arg Thr Pro Phe Thr
1   5

<210> 514
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 514
Arg Ala Ser Gln Ser Ile Tyr Pro Phe Leu Glu
1   5   10

<210> 515
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 515
Phe Thr Ser Arg Leu Gln Ser
1 5

<210> 516
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 516
Gln Gln Asn Ala Thr Asn Pro Ala Thr
1 5

<210> 517
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 517
Ser Ala Asn Met Ser
1 5

<210> 518
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 518
Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val Arg
1 5 10 15

Gly

<210> 519
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 519
Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr
1 5 10

<210> 520
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 520
Ser Ala Asn Met Ser
1 5

<210> 521
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 521
Trp Ile Glu Ala Ser Gly Val Gln Thr Phe Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 522
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 522
Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr
1 5 10

<210> 523
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 523
Thr Tyr Lys Met Val
1 5

<210> 524
<211> 17

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 524
Ser Ile Gly Pro Gly Gly Leu Asp Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 525
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 525
Ser Trp Met Thr Leu Pro Ile Thr Gly Phe Asp Tyr
1 5 10

<210> 526
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 526
Leu Tyr Glu Met Ala
1 5

<210> 527
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 527
Ser Ile Met Ser Asn Gly Ile Arg Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 528
<211> 12

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 528
Arg Lys Ser Ser Ser Ser Arg Thr Val Phe Asp Tyr
1 5 10

<210> 529
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 529
Ser Ala Asn Met Thr
1 5

<210> 530
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 530
Trp Ile Asp Asp Thr Gly Thr Gln Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 531
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 531
Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr
1 5 10

<210> 532
<211> 108
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 532
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 533
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 533
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 534
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 534
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Thr Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 535
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 535
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 536
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 536
Asp Ile Cys Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 537
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 537
Asp Ile Gln Met Thr Gln Ser Pro Cys Ser Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 538
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 538
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Cys Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 539
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 539
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Cys Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 540
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 540
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Cys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 541
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 541
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Cys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 542
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 542
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Cys Arg Phe Ser Gly

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    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 543
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 543
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Cys Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 544
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 544
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Cys Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 545
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 545
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Cys Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 546
<211> 108
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 546
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Arg His Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Cys Val Glu Ile Lys Arg
100 105

<210> 547
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 547
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 548
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 548
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Phe Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 549
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 549
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Gln Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 550
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 550
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Val Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 551
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 551
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 552
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 552

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1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ile Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 553
<211> 108
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 553
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Thr Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 554
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 554
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala

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                85                  90                  95

Thr Phe Met Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 555
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 555
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Asp Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 556
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 556
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
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```
Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95


Thr Phe Tyr Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 557
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 557
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30


Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Leu Ala Asn Pro Ala
                85                  90                  95


Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 558
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 558
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Thr Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 559
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 559
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Ala Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 560
<211> 108

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 560
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Ile Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 561
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 561
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 562
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 562
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 563
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 563
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Met Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 564
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 564
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Tyr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 565
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 565

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Gln Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 566
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 566

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Glu Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 567

<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 567
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Ile Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 568
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 568
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 569
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 569
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 570
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 570
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

```
        35                  40                  45

Tyr Phe Thr Ser Asp Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 571
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 571
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Met Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105

<210> 572
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 572
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Trp Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 573
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 573
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Arg Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 574
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 574
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Glu Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 575
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 575
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Thr Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 576
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 576
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 577
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 577
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ala Ile Trp Pro Phe
20 25 30

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Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 578
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 578
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 579
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"
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<400> 579
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Phe Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 580
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 580
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
            20   25   30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85   90   95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
            100   105

<210> 581
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 581
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Lys Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 582
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 582
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Tyr Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 583
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 583
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Pro Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Ile Ala Asn Pro Ala
85 90 95

Thr Phe Ser Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 584
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 584
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Gly Ser Arg Thr Ile Trp Pro Phe
20 25 30

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Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 585
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 585
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Thr Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105


<210> 586
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
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polypeptide"

<400> 586
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Thr Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 587
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 587
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 588
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 588
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 589
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 589
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 590
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 590
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 591
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 591
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

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Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 592
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 592

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Thr Ile Trp Pro Phe
            20                  25                  30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
                85                  90                  95

Thr Phe Ala Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
```

<210> 593
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 593
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 594
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 594
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Thr Gln Gly Thr Lys Val Glu Ile Lys Arg

100 105

<210> 595
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 595
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asn Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 596
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 596
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Ser Ile Trp Pro Phe
20 25 30

Leu Glu Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Thr Leu Ala Ala Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asn Val Ala Asn Pro Ala
85 90 95

Thr Phe Pro Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 597
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 597
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 598
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 598
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Ser Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 599
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 599
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Gln Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 600
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 600
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 601
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 601
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

```
Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

His Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 602
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 602

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Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Phe Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 603

<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 603
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Leu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 604
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 604
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Pro Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 605
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 605
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ala Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 606
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 606
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Trp Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 607
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 607
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Glu Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 608
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 608
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ser Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 609
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 609
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

```
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Gly Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 610
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 610
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Lys Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
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115 120

<210> 611
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 611
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Thr Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 612
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 612
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Ala Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 613
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 613
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Glu Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 614
<211> 120
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 614
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Arg Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 615
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 615
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Pro Phe Gly Phe Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 616
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 616
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30


Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60


Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Thr Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 617
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 617
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```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Val Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 618
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 618

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Leu Gly Gln
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100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 619
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 619
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 620
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 620
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

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Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Phe Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 621
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 621
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Ser Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120
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<210> 622
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 622
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Met Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 623
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 623
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Lys Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 624
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 624
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr His Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 625
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 625
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Ile Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 626
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 626
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

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                85                  90                  95

Ala Arg Ser Pro Leu Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 627
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 627
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Arg Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 628
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 628
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15
```

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Tyr Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 629
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 629
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20                  25                  30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50                  55                  60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Gln Gly Gln
            100                 105                 110
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Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 630
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 630
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
    50   55   60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Ser Pro Arg Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 631
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 631
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
            20   25   30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Pro Met Gly Ile Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 632
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 632
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro His Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 633
<211> 120
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 633
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Met Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 634
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 634
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Phe Gly Ala Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 635
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 635
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Ser Ala
20 25 30

Asn Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Trp Ile Glu Ala Pro Gly Val Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Lys Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 636
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 636
Arg Ala Ser Arg Pro Ile Trp Pro Phe Leu Glu
1   5   10

<210> 637
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 637
Phe Thr Ser Arg Leu Arg His
1   5

<210> 638
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 638
Leu Gln Asn Val Ala Asn Pro Ala Thr
1   5

<210> 639
<211> 6
<212> PRT
<213> Homo sapiens

<400> 639
Met Tyr Pro Pro Pro Tyr
1   5

<210> 640
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 640
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Met Arg Ala
            20   25   30

Asn Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Trp Ile Glu Asp Thr Gly Thr Gln Thr Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Pro Phe Gly Pro Leu Tyr Gly Phe Asp Tyr Arg Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 641
<211> 98
<212> PRT
<213> Homo sapiens

<400> 641
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys

<210> 642
<211> 287
<212> DNA
<213> Homo sapiens

<400> 642
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagta cccctcc 287

<210> 643
<211> 95
<212> PRT
<213> Homo sapiens

<400> 643
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro
85 90 95

<210> 644
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic 6xHis tag"

<400> 644
His His His His His His
1 5