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(54) Title: MULTIMERIC T-CELL MODULATORY POLYPEPTIDES AND METHODS OF USE THEREOF

(57) Abstract: The present disclosure provides T-cell modulatory multimeric polypeptides that comprise an immunomodulatory polypeptide, an epitope-presenting peptide, and class I MHC polypeptides. A T-cell modulatory multimeric polypeptide is useful for modulating the activity of a T cell, and for modulating an immune response in an individual.

MULTIMERIC T-CELL MODULATORY POLYPEPTIDES AND METHODS OF USE THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/782,205, filed December 19, 2018, and U.S. Provisional Patent Application No. 62/814,707, filed March 6, 2019, which applications are incorporated herein by reference in their entirety.

INTRODUCTION

[0002] An adaptive immune response involves the engagement of the T cell receptor (TCR), present on the surface of a T cell, with a small peptide antigen non-covalently presented on the surface of an antigen presenting cell (APC) by a major histocompatibility complex (MHC; also referred to in humans as a human leukocyte antigen (HLA) complex). This engagement represents the immune system's targeting mechanism and is a requisite molecular interaction for T cell modulation (activation or inhibition) and effector function. Following epitope-specific cell targeting, the targeted T cells are activated through engagement of costimulatory proteins found on the APC with counterpart costimulatory proteins the T cells. Both signals – epitope/TCR binding and engagement of APC costimulatory proteins with T cell costimulatory proteins – are required to drive T cell specificity and activation or inhibition. The TCR is specific for a given epitope; however, the costimulatory protein not epitope specific and instead is generally expressed on all T cells or on large T cell subsets.

SUMMARY

[0003] The present disclosure provides T-cell modulatory multimeric polypeptides (TMMPs) that comprise an immunomodulatory polypeptide, class I HLA polypeptides (a class I HLA heavy chain polypeptide and a β2 microglobulin polypeptide), and a peptide that presents an epitope to a T-cell receptor. A TMMP is useful for modulating the activity of a T cell, and for modulating an immune response in an individual.

BRIEF DESCRIPTION OF THE DRAWINGS

[0001] **FIGs. 1A-1F** are schematic depictions of various TMMPs of the present disclosure.

[0002] **FIGs. 2A-2F** are schematic depictions of various disulfide-linked TMMPs of the present disclosure.

[0003] **FIGs. 3A-3G** provide amino acid sequences of immunoglobulin Fc polypeptides. The sequences of FIGs. 5A-5G are set forth in SEQ ID NOs: 449-460, respectively.

[0004] **FIG. 4** provides a multiple amino acid sequence alignment of beta-2 microglobulin (β2M) precursors (i.e., including the leader sequence) from *Homo sapiens* (NP_004039.1; SEQ ID NO:19), *Pan troglodytes* (NP_001009066.1; SEQ ID NO:19), *Macaca mulatta* (NP_001040602.1; SEQ ID NO:20), *Bos taurus* (NP_776318.1; SEQ ID NO:21) and *Mus musculus* (NP_033865.2; SEQ ID NO:22). Amino acids 1-20 are a signal peptide.

[0005] **FIGs. 5A-5C** provide amino acid sequences of full-length human HLA heavy chains of alleles A*0101 (SEQ ID NO: 23), A*1101 (SEQ ID NO: 24), A*2402 (SEQ ID NO: 25), and A*3303 (SEQ ID NO: 26) (FIG. 7A); full-length human HLA heavy chain of allele B*0702 (SEQ ID NO: 27) (FIG. 5B); and a full-length human HLA-C heavy chain (SEQ ID NO: 28) (FIG. 5C).

[0006] **FIG. 6** provides an alignment of eleven mature MHC class I heavy chain amino acid sequences without their leader sequences, transmembrane domains, and intracellular domains. Top to bottom: SEQ ID NOs: 41-51.

[0007] **FIGs. 7A-7B** provide an alignment of HLA-A heavy chain amino acid sequences (FIG. 7A; SEQ ID NOs: 198-206, respectively) and a consensus sequence (FIG. 7B; SEQ ID NO: 29).

[0008] **FIGs. 8A-8B** provide an alignment of HLA-B heavy chain amino acid sequences (FIG. 8A; SEQ ID NOs: 207-213, respectively) and a consensus sequence (FIG. 8B; SEQ ID NO: 30).

[0009] **FIGs. 9A-9B** provide an alignment of HLA-C heavy chain amino acid sequences (FIG. 9A; SEQ ID NOs: 214-222, respectively) and a consensus sequence (FIG. 9B; SEQ ID NO: 31).

[0010] **FIG. 10** provides a consensus amino acid sequence for each of HLA-E, -F, and -G heavy chains (SEQ ID NOs:32-34, respectively). Variable amino acid (aa) positions are indicated as "X" residues sequentially numbered; the locations of amino acids 84, 139, and 236 are double underlined.

[0011] **FIG. 11** provides an alignment of consensus amino acid sequences for HLA-A (SEQ ID NO: 35), -B (SEQ ID NO: 36), -C (SEQ ID NO: 37), -E (SEQ ID NO: 38), -F (SEQ ID NO: 39), and -G (SEQ ID NO: 40).

[0012] **FIG. 12A-12D** provide schematic depictions of multiple disulfide-linked TMMP of the present disclosure.

[0013] **FIG. 13A-13C** provide schematic depictions of examples of configurations of disulfide-linked TMMPs of the present disclosure.

[0014] **FIG. 14** provide schematic depictions of examples of positions of immunomodulatory polypeptides in TMMPs of the present disclosure.

DEFINITIONS

[0015] The terms "polynucleotide" and "nucleic acid," used interchangeably herein, refer to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. Thus, this

term includes, but is not limited to, single-, double-, or multi-stranded DNA or RNA, genomic DNA, cDNA, DNA-RNA hybrids, or a polymer comprising purine and pyrimidine bases or other natural, chemically or biochemically modified, non-natural, or derivatized nucleotide bases.

[0016] The terms "peptide," "polypeptide," and "protein" are used interchangeably herein, and refer to a polymeric form of amino acids of any length, which can include coded and non-coded amino acids, chemically or biochemically modified or derivatized amino acids, and polypeptides having modified peptide backbones.

[0017] A polynucleotide or polypeptide has a certain percent "sequence identity" to another polynucleotide or polypeptide, meaning that, when aligned, that percentage of bases or amino acids are the same, and in the same relative position, when comparing the two sequences. Sequence identity can be determined in a number of different ways. To determine sequence identity, sequences can be aligned using various convenient methods and computer programs (e.g., BLAST, T-COFFEE, MUSCLE, MAFFT, etc.), available over the world wide web at sites including ncbi.nlm.nili.gov/BLAST, ebi.ac.uk/Tools/msa/tcoffee/, ebi.ac.uk/Tools/msa/muscle/, mafft.cbrc.jp/alignment/software/. See, e.g., Altschul et al. (1990), J. Mol. Bioi. 215:403-10.

[0018] The term "conservative amino acid substitution" refers to the interchangeability in proteins of amino acid residues having similar side chains. For example, a group of amino acids having aliphatic side chains consists of glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains consists of serine and threonine; a group of amino acids having amide containing side chains consisting of asparagine and glutamine; a group of amino acids having aromatic side chains consists of phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains consists of lysine, arginine, and histidine; a group of amino acids having acidic side chains consists of glutamate and aspartate; and a group of amino acids having sulfur containing side chains consists of cysteine and methionine. Exemplary conservative amino acid substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine-glycine, and asparagine-glutamine.

[0019] The term “immunological synapse” or “immune synapse” as used herein generally refers to the natural interface between two interacting immune cells of an adaptive immune response including, e.g., the interface between an antigen-presenting cell (APC) or target cell and an effector cell, e.g., a lymphocyte, an effector T cell, a natural killer cell, and the like. An immunological synapse between an APC and a T cell is generally initiated by the interaction of a T cell antigen receptor and major histocompatibility complex molecules, e.g., as described in Bromley et al., Annu Rev Immunol. 2001;19:375-96; the disclosure of which is incorporated herein by reference in its entirety.

[0020] "T cell" includes all types of immune cells expressing CD3, including T-helper cells ($CD4^+$ cells), cytotoxic T-cells ($CD8^+$ cells), T-regulatory cells (Treg), and NK-T cells.

[0021] The term "immunomodulatory polypeptide" (also referred to as a "co-stimulatory polypeptide"), as used herein, includes a polypeptide on an antigen presenting cell (APC) (e.g., a dendritic cell, a B cell, and the like) that specifically binds a cognate co-immunomodulatory polypeptide on a T cell, thereby providing a signal which, in addition to the primary signal provided by, for instance, binding of a TCR/CD3 complex with a major histocompatibility complex (MHC) polypeptide loaded with peptide, mediates a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like. An immunomodulatory polypeptide can include, but is not limited to, CD7, B7-1 (CD80), B7-2 (CD86), PD-L1, PD-L2, 4-1BBL, OX40L, Fas ligand (FasL), inducible costimulatory ligand (ICOS-L), intercellular adhesion molecule (ICAM), CD30L, CD40, CD70, CD83, HLA-G, MICA, MICB, HVEM, lymphotoxin beta receptor, 3/TR6, ILT3, ILT4, HVEM, an agonist or antibody that binds Toll ligand receptor and a ligand that specifically binds with B7-H3.

[0022] As noted above, an "immunomodulatory polypeptide" (also referred to herein as a "MOD") specifically binds a cognate co-immunomodulatory polypeptide on a T cell.

[0023] An "immunomodulatory domain" ("MOD") of a TMMP of the present disclosure binds a cognate co-immunomodulatory polypeptide, which may be present on a target T cell.

[0024] "Heterologous," as used herein, means a nucleotide or polypeptide that is not found in the native nucleic acid or protein, respectively.

[0025] "Recombinant," as used herein, means that a particular nucleic acid (DNA or RNA) is the product of various combinations of cloning, restriction, polymerase chain reaction (PCR) and/or ligation steps resulting in a construct having a structural coding or non-coding sequence distinguishable from endogenous nucleic acids found in natural systems. DNA sequences encoding polypeptides can be assembled from cDNA fragments or from a series of synthetic oligonucleotides, to provide a synthetic nucleic acid which is capable of being expressed from a recombinant transcriptional unit contained in a cell or in a cell-free transcription and translation system.

[0026] The terms "recombinant expression vector," or "DNA construct" are used interchangeably herein to refer to a DNA molecule comprising a vector and at least one insert. Recombinant expression vectors are usually generated for the purpose of expressing and/or propagating the insert(s), or for the construction of other recombinant nucleotide sequences. The insert(s) may or may not be operably linked to a promoter sequence and may or may not be operably linked to DNA regulatory sequences.

[0027] As used herein, the term "affinity" refers to the equilibrium constant for the reversible binding of two agents (e.g., an antibody and an antigen) and is expressed as a dissociation constant (K_D).

Affinity can be at least 1-fold greater, at least 2-fold greater, at least 3-fold greater, at least 4-fold greater, at least 5-fold greater, at least 6-fold greater, at least 7-fold greater, at least 8-fold greater, at least 9-fold greater, at least 10-fold greater, at least 20-fold greater, at least 30-fold greater, at least 40-fold greater, at least 50-fold greater, at least 60-fold greater, at least 70-fold greater, at least 80-fold greater, at least 90-fold greater, at least 100-fold greater, or at least 1,000-fold greater, or more, than the affinity of an antibody for unrelated amino acid sequences. Affinity of an antibody to a target protein can be, for example, from about 100 nanomolar (nM) to about 0.1 nM, from about 100 nM to about 1 picomolar (pM), or from about 100 nM to about 1 femtomolar (fM) or more. As used herein, the term "avidity" refers to the resistance of a complex of two or more agents to dissociation after dilution. The terms "immunoreactive" and "preferentially binds" are used interchangeably herein with respect to antibodies and/or antigen-binding fragments.

[0028] The term "binding," as used herein (e.g. with reference to binding of a TMMP to a polypeptide (e.g., a T-cell receptor) on a T cell), refers to a non-covalent interaction between two molecules. Non-covalent binding refers to a direct association between two molecules, due to, for example, electrostatic, hydrophobic, ionic, and/or hydrogen-bond interactions, including interactions such as salt bridges and water bridges. Non-covalent binding interactions are generally characterized by a dissociation constant (K_D) of less than 10^{-6} M, less than 10^{-7} M, less than 10^{-8} M, less than 10^{-9} M, less than 10^{-10} M, less than 10^{-11} M, less than 10^{-12} M, less than 10^{-13} M, less than 10^{-14} M, or less than 10^{-15} M. "Affinity" refers to the strength of non-covalent binding, increased binding affinity being correlated with a lower K_D. "Specific binding" generally refers to binding with an affinity of at least about 10^{-7} M or greater, *e.g.*, 5x 10^{-7} M, 10^{-8} M, 5 x 10^{-8} M, 10^{-9} M, and greater. "Non-specific binding" generally refers to binding (e.g., the binding of a ligand to a moiety other than its designated binding site or receptor) with an affinity of less than about 10^{-7} M (*e.g.*, binding with an affinity of 10^{-6} M, 10^{-5} M, 10^{-4} M). However, in some contexts, e.g., binding between a TCR and a peptide/MHC complex, "specific binding" can be in the range of from 1 μM to 100 μM, or from 100 μM to 1 mM. "Covalent binding" or "covalent bond," as used herein, refers to the formation of one or more covalent chemical binds between two different molecules.

[0029] The terms "treatment", "treating" and the like are used herein to generally mean obtaining a desired pharmacologic and/or physiologic effect. The effect may be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or may be therapeutic in terms of a partial or complete cure for a disease and/or adverse effect attributable to the disease. "Treatment" as used herein covers any treatment of a disease or symptom in a mammal, and includes: (a) preventing the disease or symptom from occurring in a subject which may be predisposed to acquiring the disease or symptom but has not yet been diagnosed as having it; (b) inhibiting the disease or symptom, i.e., arresting its development; and/or (c) relieving the disease, i.e., causing regression of the disease. The

therapeutic agent may be administered before, during or after the onset of disease or injury. The treatment of ongoing disease, where the treatment stabilizes or reduces the undesirable clinical symptoms of the patient, is of particular interest. Such treatment is desirably performed prior to complete loss of function in the affected tissues. The subject therapy will desirably be administered during the symptomatic stage of the disease, and in some cases after the symptomatic stage of the disease.

[0030] The terms "individual," "subject," "host," and "patient," are used interchangeably herein and refer to any mammalian subject for whom diagnosis, treatment, or therapy is desired. Mammals include, e.g., humans, non-human primates, rodents (e.g., rats; mice), lagomorphs (e.g., rabbits), ungulates (e.g., cows, sheep, pigs, horses, goats, and the like), etc.

[0031] Before the present invention is further described, it is to be understood that this invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0032] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

[0033] 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 to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited.

[0034] It must be noted that as used herein and in the appended claims, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to a “T-cell modulatory multimeric polypeptide” includes a plurality of such polypeptides and reference to “the immunomodulatory polypeptide” includes reference to one or more immunomodulatory polypeptides and equivalents thereof known to those skilled in the art, and so forth. It is further noted that the claims may be drafted to exclude any optional element. As such, this statement is intended to

serve as antecedent basis for use of such exclusive terminology as "solely," "only" and the like in connection with the recitation of claim elements, or use of a "negative" limitation.

[0035] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. All combinations of the embodiments pertaining to the invention are specifically embraced by the present invention and are disclosed herein just as if each and every combination was individually and explicitly disclosed. In addition, all sub-combinations of the various embodiments and elements thereof are also specifically embraced by the present invention and are disclosed herein just as if each and every such sub-combination was individually and explicitly disclosed herein.

[0036] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed.

DETAILED DESCRIPTION

[0037] The present disclosure provides T-cell modulatory multimeric polypeptides that comprise an immunomodulatory polypeptide and that comprise an epitope-presenting peptide. A TMMP is useful for modulating the activity of a T cell, and for modulating an immune response in an individual.

T-CELL MODULATORY MULTIMERIC POLYPEPTIDES

[0038] The present disclosure provides a T-cell modulatory multimeric polypeptide (TMMP) comprising: a) a first polypeptide; and b) a second polypeptide, wherein the TMMP comprises an epitope; a first major histocompatibility complex (MHC) polypeptide; a second MHC polypeptide; one or more immunomodulatory polypeptides; and optionally an immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold. The present disclosure provides a TMMP, wherein the TMMP is a heterodimer comprising: a) a first polypeptide comprising a first MHC polypeptide; and b) a second polypeptide comprising a second MHC polypeptide, wherein the first polypeptide or the second polypeptide comprises an epitope (e.g., a peptide that presents an epitope); wherein the first polypeptide and/or the second polypeptide comprises one or more immunomodulatory polypeptides that can be the same or different; and optionally an Ig F c polypeptide or a non-Ig scaffold. A TMMP of the present disclosure is also referred to herein as a "multimeric polypeptide of the present disclosure" or a "synTac." In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In

some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[0039] The present disclosure provides a TMMP comprising a heterodimeric polypeptide comprising: a) a first polypeptide comprising: i) a peptide epitope; and ii) a first MHC polypeptide; b) a second polypeptide comprising a second MHC polypeptide; and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the at least one (i.e., one or more) immunomodulatory polypeptide. Optionally, the first or the second polypeptide comprises an Ig Fc polypeptide or a non-Ig scaffold. At least one of the one or more immunomodulatory polypeptides is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide. The epitope present in a TMMP of the present disclosure binds to a T-cell receptor (TCR) on a T cell with an affinity of at least 100 μM (e.g., at least 10 μM, at least 1 μM, at least 100 nM, at least 10 nM, or at least 1 nM). A TMMP of the present disclosure binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the TMMP binds a second T cell, where the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 100 μM, and where the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 100 μM (e.g., at least 10 μM, at least 1 μM, at least 100 nM, at least 10 nM, or at least 1 nM). In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[0040] The present disclosure provides a TMMP, wherein the TMMP is:

[0041] A) a heterodimer comprising: a) a first polypeptide comprising a first MHC polypeptide; and b) a second polypeptide comprising a second MHC polypeptide, wherein the first polypeptide or the second polypeptide comprises an epitope (e.g., a peptide that comprises an epitope recognized by a T cell); wherein the first polypeptide and/or the second polypeptide comprises one or more immunomodulatory polypeptides that can be the same or different, and wherein at least one of the one or more immunomodulatory polypeptides may be a wild-type immunomodulatory polypeptide or a variant of a wild-type immunomodulatory polypeptide, wherein the variant immunomodulatory polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions compared to the amino acid sequence of the corresponding wild-type immunomodulatory polypeptide; and wherein the first polypeptide or the second polypeptide optionally comprises an Ig Fc polypeptide or a non-Ig scaffold; or

[0042] B) a heterodimer comprising: a) a first polypeptide comprising a first MHC polypeptide; and b) a second polypeptide comprising a second MHC polypeptide, wherein the first polypeptide or the second polypeptide comprises an epitope; wherein the first polypeptide and/or the second polypeptide comprises one or more immunomodulatory polypeptides that can be the same or different,

[0043] wherein at least one of the one or more immunomodulatory polypeptides is a variant of a wild-type immunomodulatory polypeptide, wherein the variant immunomodulatory polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions compared to the amino acid sequence of the corresponding wild-type immunomodulatory polypeptide,

[0044] wherein at least one of the one or more immunomodulatory domains is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide, and wherein the epitope binds to a TCR on a T cell with an affinity of at least 10^{-7} M, such that: i) the TMMP polypeptide binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the TMMP binds a second T cell, wherein the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 10^{-7} M, and wherein the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 10^{-7} M; and/or ii) the ratio of the binding affinity of a control TMMP, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the TMMP comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is in a range of from 1.5:1 to 10^6:1; and wherein the variant immunomodulatory polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions compared to the amino acid sequence of the corresponding wild-type immunomodulatory polypeptide; and

[0045] wherein the first polypeptide or the second polypeptide optionally comprises an Ig Fc polypeptide or a non-Ig scaffold; or

[0046] C) a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) an epitope; ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; and ii) optionally an immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold, wherein the TMMP comprises one or more immunomodulatory domains that can be the same or different, wherein at least one of the one or more immunomodulatory domain is: A) at the C-terminus of the first polypeptide; B) at the N-terminus of the second polypeptide; C) at the C-terminus of the second polypeptide; or D) at the C-terminus of the first

polypeptide and at the N-terminus of the second polypeptide, and wherein at least one of the one or more immunomodulatory domains may be a wild-type immunomodulatory polypeptide or a variant of a wild-type immunomodulatory polypeptide, wherein the variant immunomodulatory polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions compared to the amino acid sequence of the corresponding wild-type immunomodulatory polypeptide; and

[0047] optionally wherein at least one of the one or more immunomodulatory domains is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide, and wherein the epitope binds to a TCR on a T cell with an affinity of at least 10^{-7} M, such that: i) the TMMP binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the TMMP binds a second T cell, wherein the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 10^{-7} M, and wherein the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 10^{-7} M; and/or ii) the ratio of the binding affinity of a control TMMP, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the TMMP comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is in a range of from 1.5:1 to 10^6:1; and wherein the variant immunomodulatory polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9,10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions compared to the amino acid sequence of the corresponding wild-type immunomodulatory polypeptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[0048] The present disclosure provides a TMMP comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) an epitope; ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; and ii) optionally an Ig Fc polypeptide or a non-Ig scaffold. A TMMP of the present disclosure comprises one or more immunomodulatory polypeptides, wherein at least one of the one or more immunomodulatory polypeptides is: A) at the C-terminus of the first polypeptide; B) at the N-terminus of the second polypeptide; C) at the C-terminus of the second polypeptide; or D) at the C-terminus of the first polypeptide and at the N-terminus of the second polypeptide. At least one of the one or more immunomodulatory polypeptides is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding

wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide. The epitope present in a TMMP of the present disclosure binds to a T-cell receptor (TCR) on a T cell with an affinity of at least 100 μM (e.g., at least 10 μM, at least 1 μM, at least 100 nM, at least 10 nM, or at least 1 nM). A TMMP of the present disclosure binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the TMMP binds a second T cell, where the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 100 μM, and where the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 100 μM (e.g., at least 10 μM, at least 1 μM, at least 100 nM, at least 10 nM, or at least 1 nM).

[0049] In some cases, the epitope present in a TMMP of the present disclosure binds to a TCR on a T cell with an affinity of from about 10^{-4} M to about 5 x 10^{-4} M, from about 5 x 10^{-4} M to about 10^{-5} M, from about 10^{-5} M to 5 x 10^{-5} M, from about 5 x 10^{-5} M to 10^{-6} M, from about 10^{-6} M to about 5 x 10^{-6} M, from about 5 x 10^{-6} M to about 10^{-7} M, from about 10^{-7} M to about 5 x 10^{-7} M, from about 5 x 10^{-7} M to about 10^{-8} M, or from about 10^{-8} M to about 10^{-9} M. Expressed another way, in some cases, the epitope present in a TMMP of the present disclosure binds to a TCR on a T cell with an affinity of from about 1 nM to about 5 nM, from about 5 nM to about 10 nM, from about 10 nM to about 50 nM, from about 50 nM to about 100 nM, from about 0.1 μM to about 0.5 μM, from about 0.5 μM to about 1 μM, from about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, from about 75 μM to about 100 μM.

[0050] An immunomodulatory polypeptide present in a TMMP of the present disclosure binds to its cognate co-immunomodulatory polypeptide with an affinity that it at least 10% less, at least 15% less, at least 20% less, at least 25% less, at least 30% less, at least 35% less, at least 40% less, at least 45% less, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide.

[0051] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure has a binding affinity for a cognate co-immunomodulatory polypeptide that is from 1 nM to 100 nM, or from 100 nM to 100 μM. For example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure has a binding affinity for a cognate co-immunomodulatory polypeptide that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM,

from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM. In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure has a binding affinity for a cognate co-immunomodulatory polypeptide that is from about 1 nM to about 5 nM, from about 5 nM to about 10 nM, from about 10 nM to about 50 nM, from about 50 nM to about 100 nM.

[0052] The combination of the reduced affinity of the immunomodulatory polypeptide for its cognate co-immunomodulatory polypeptide, and the affinity of the epitope for a TCR, provides for enhanced selectivity of a TMMP of the present disclosure. For example, a TMMP of the present disclosure binds selectively to a first T cell that displays both: i) a TCR specific for the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP, compared to binding to a second T cell that displays: i) a TCR specific for an epitope other than the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP. For example, a TMMP of the present disclosure binds to the first T cell with an affinity that is at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 2-fold, at least 2.5-fold, at least 5-fold, at least 10-fold, at least 15-fold, at least 20-fold, at least 25-fold, at least 50-fold, at least 100-fold, or more than 100-fold, higher than the affinity to which it binds the second T cell.

[0053] In some cases, a TMMP of the present disclosure, when administered to an individual in need thereof, induces both an epitope-specific T cell response and an epitope non-specific T cell response. In other words, in some cases, a TMMP of the present disclosure, when administered to an individual in need thereof, induces an epitope-specific T cell response by modulating the activity of a first T cell that displays both: i) a TCR specific for the epitope present in the TMMP; ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP; and induces an epitope non-specific T cell response by modulating the activity of a second T cell that displays: i) a TCR specific for an epitope other than the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP. The ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, or at least 100:1. The ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is from about 2:1 to about 5:1, from about 5:1 to about 10:1, from about 10:1 to about 15:1, from about 15:1 to about 20:1, from about 20:1 to about 25:1, from about 25:1 to about 50:1, or from about 50:1 to about 100:1, or more than 100:1. "Modulating the activity" of a T cell can include one or more of: i) activating a cytotoxic

(e.g., $CD8^+$) T cell; ii) inducing cytotoxic activity of a cytotoxic (e.g., $CD8^+$) T cell; iii) inducing production and release of a cytotoxin (e.g., a perforin; a granzyme; a granulysin) by a cytotoxic (e.g., $CD8^+$) T cell; iv) inhibiting activity of an autoreactive T cell; and the like.

[0054] The combination of the reduced affinity of the immunomodulatory polypeptide for its cognate co-immunomodulatory polypeptide, and the affinity of the epitope for a TCR, provides for enhanced selectivity of a TMMP of the present disclosure. Thus, for example, a TMMP of the present disclosure binds with higher avidity to a first T cell that displays both: i) a TCR specific for the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP, compared to the avidity to which it binds to a second T cell that displays: i) a TCR specific for an epitope other than the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP.

[0055] Binding affinity between an immunomodulatory polypeptide and its cognate co-immunomodulatory polypeptide can be determined by bio-layer interferometry (BLI) using purified immunomodulatory polypeptide and purified cognate co-immunomodulatory polypeptide. Binding affinity between a TMMP and its cognate co-immunomodulatory polypeptide can be determined by BLI using purified TMMP and the cognate co-immunomodulatory polypeptide. BLI methods are well known to those skilled in the art. See, e.g., Lad et al. (2015) *J. Biomol. Screen.* 20(4):498-507; and Shah and Duncan (2014) *J. Vis. Exp.* 18:e51383.

[0056] A BLI assay can be carried out using an Octet RED 96 (Pal FortéBio) instrument, or a similar instrument, as follows. A TMMP (e.g., a TMMP of the present disclosure; a control TMMP (where a control TMMP comprises a wild-type immunomodulatory polypeptide)) is immobilized onto an insoluble support (a "biosensor"). The immobilized TMMP is the "target." Immobilization can be effected by immobilizing a capture antibody onto the insoluble support, where the capture antibody immobilizes the TMMP. For example, immobilization can be effected by immobilizing anti-Fc (e.g., anti-human IgG Fc) antibodies onto the insoluble support, where the immobilized anti-Fc antibodies bind to and immobilize the TMMP (where the TMMP comprises an IgFc polypeptide). A co-immunomodulatory polypeptide is applied, at several different concentrations, to the immobilized TMMP, and the instrument's response recorded. Assays are conducted in a liquid medium comprising 25mM HEPES pH 6.8, 5% poly(ethylene glycol) 6000, 50 mM KCl, 0.1% bovine serum albumin, and 0.02% Tween 20 nonionic detergent. Binding of the co-immunomodulatory polypeptide to the immobilized TMMP is conducted at 30°C. As a positive control for binding affinity, an anti-MHC Class I monoclonal antibody can be used. For example, anti-HLA Class I monoclonal antibody W6/32 (American Type Culture Collection No. HB-95; Parham et al. (1979) *J. Immunol.* 123:342), which has a K_D of 7 nM, can be used. A standard curve can be generated using serial dilutions of the anti-MHC Class I monoclonal antibody. The co-immunomodulatory polypeptide, or the anti-MHC Class I mAb, is the

"analyte." BLI analyzes the interference pattern of white light reflected from two surfaces: i) from the immobilized polypeptide ("target"); and ii) an internal reference layer. A change in the number of molecules ("analyte"; e.g., co-immunomodulatory polypeptide; anti-HLA antibody) bound to the biosensor tip causes a shift in the interference pattern; this shift in interference pattern can be measured in real time. The two kinetic terms that describe the affinity of the target/analyte interaction are the association constant (k_a) and dissociation constant (k_d). The ratio of these two terms ($k_d/_a$) gives rise to the affinity constant K_D.

[0057] The BLI assay is carried out in a multi-well plate. To run the assay, the plate layout is defined, the assay steps are defined, and biosensors are assigned in Octet Data Acquisition software. The biosensor assembly is hydrated. The hydrated biosensor assembly and the assay plate are equilibrated for 10 minutes on the Octet instrument. Once the data are acquired, the acquired data are loaded into the Octet Data Analysis software. The data are processed in the Processing window by specifying method for reference subtraction, y-axis alignment, inter-step correction, and Savitzky-Golay filtering. Data are analyzed in the Analysis window by specifying steps to analyze (Association and Dissociation), selecting curve fit model (1:1), fitting method (global), and window of interest (in seconds). The quality of fit is evaluated. K_D values for each data trace (analyte concentration) can be averaged if within a 3-fold range. K_D error values should be within one order of magnitude of the affinity constant values; R^2 values should be above 0.95. See, e.g., Abdiche et al. (2008) *J. Anal. Biochem.* 377:209.

[0058] Unless otherwise stated herein, the affinity of a TMMP of the present disclosure for a cognate co-immunomodulatory polypeptide, or the affinity of a control TMMP (where a control TMMP comprises a wild-type immunomodulatory polypeptide) for a cognate co-immunomodulatory polypeptide, is determined using BLI, as described above.

[0059] In some cases, the ratio of: i) the binding affinity of a control TMMP (where the control comprises a wild-type immunomodulatory polypeptide) to a cognate co-immunomodulatory polypeptide to ii) the binding affinity of a TMMP of the present disclosure comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by BLI (as described above), is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1. In some cases, the ratio of: i) the binding affinity of a control TMMP (where the control comprises a wild-type immunomodulatory polypeptide) to a cognate co-immunomodulatory polypeptide to ii) the binding affinity of a TMMP of the present disclosure comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by BLI, is in a range of from 1.5:1 to 10^6:1, e.g., from 1.5:1 to 10:1, from 10:1 to 50:1, from 50:1 to 10^2:1, from 10^2:1 to 10^3:1, from10^3:1 to 10^4:1, from 10^4:1 to 10^5:1, or from 10^5:1 to 10^6:1.

[0060] As an example, where a control TMMP comprises a wild-type IL-2 polypeptide, and where a TMMP of the present disclosure comprises a variant IL-2 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type IL-2 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to an IL-2 receptor (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the IL-2 receptor, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1. In some cases, where a control TMMP comprises a wild-type IL-2 polypeptide, and where a TMMP of the present disclosure comprises a variant IL-2 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type IL-2 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to an IL-2 receptor (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the IL-2 receptor, when measured by BLI, is in a range of from 1.5:1 to 10^6:1, e.g., from 1.5:1 to 10:1, from 10:1 to 50:1, from 50:1 to 10^2:1, from 10^2:1 to 10^3:1, from10^3:1 to 10^4:1, from 10^4:1 to 10^5:1, or from 10^5:1 to 10^6:1.

[0061] As another example, where a control TMMP comprises a wild-type PD-L1 polypeptide, and where a TMMP of the present disclosure comprises a variant PD-L1 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type PD-L1 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to a PD-1 polypeptide (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the PD-1 polypeptide, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1.

[0062] As another example, where a control TMMP comprises a wild-type CD80 polypeptide, and where a TMMP of the present disclosure comprises a variant CD80 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type CD80 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to a CTLA4 polypeptide (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the CTLA4 polypeptide, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1.

[0063] As another example, where a control TMMP comprises a wild-type CD80 polypeptide, and where a TMMP of the present disclosure comprises a variant CD80 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type CD80 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to a CD28 polypeptide (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the CD28 polypeptide, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1.

[0064] As another example, where a control TMMP comprises a wild-type 4-1BBL polypeptide, and where a TMMP of the present disclosure comprises a variant 4-1BBL polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type 4-1BBL polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to a 4-1BB polypeptide (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the 4-1BB polypeptide, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1.

[0065] As another example, where a control TMMP comprises a wild-type CD86 polypeptide, and where a TMMP of the present disclosure comprises a variant CD86 polypeptide (comprising from 1 to 10 amino acid substitutions relative to the amino acid sequence of the wild-type CD86 polypeptide) as the immunomodulatory polypeptide, the ratio of: i) the binding affinity of the control TMMP to a CD28 polypeptide (i.e., the cognate co-immunomodulatory polypeptide) to ii) the binding affinity of the TMMP of the present disclosure to the CD28 polypeptide, when measured by BLI, is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at least 10^5:1, or at least 10^6:1.

[0066] Binding affinity of a TMMP of the present disclosure to a target T cell can be measured in the following manner: A) contacting a TMMP of the present disclosure with a target T-cell expressing on its surface: i) a cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to the epitope, where the TMMP comprises an epitope tag, such that the TMMP binds to the target T-cell; B) contacting the target T-cell-bound TMMP with a fluorescently labeled binding agent (e.g., a fluorescently labeled antibody) that binds to the epitope tag, generating a TMMP/target T-cell/binding agent complex; C) measuring the mean fluorescence intensity (MFI) of the TMMP/target T-cell/binding agent complex using flow

cytometry. The epitope tag can be, e.g., a FLAG tag, a hemagglutinin tag, a c-myc tag, a poly(histidine) tag, etc. The MFI measured over a range of concentrations of the TMMP library member provides a measure of the affinity. The MFI measured over a range of concentrations of the TMMP library member provides a half maximal effective concentration (EC_{50}) of the TMMP. In some cases, the EC_{50} of a TMMP of the present disclosure for a target T cell is in the nM range; and the EC_{50} of the TMMP for a control T cell (where a control T cell expresses on its surface: i) a cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that does not bind to the epitope present in the TMMP) is in the μM range. In some cases, the ratio of the EC_{50} of a TMMP of the present disclosure for a control T cell to the EC_{50} of the TMMP for a target T cell is at least 1.5:1, at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, at least 100:1, at least 500:1, at least 10^2:1, at least 5 x 10^2:1, at least 10^3:1, at least 5 x 10^3:1, at least 10^4:1, at lease 10^5:1, or at least 10^6:1. The ratio of the EC_{50} of a TMMP of the present disclosure for a control T cell to the EC_{50} of the TMMP for a target T cell is an expression of the selectivity of the TMMP.

[0067] In some cases, when measured as described in the preceding paragraph, a TMMP of the present disclosure exhibits selective binding to target T-cell, compared to binding of the TMMP library member to a control T cell that comprises: i) the cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to an epitope other than the epitope present in the TMMP library member.

Dimerized TMMPs

[0068] A TMMP of the present disclosure can be dimerized; i.e., the present disclosure provides a multimeric polypeptide comprising a dimer of a TMMP of the present disclosure. Thus, the present disclosure provides a TMMP comprising: A) a first heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; and ii) a first major histocompatibility complex (MHC) polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide, wherein the first heterodimer comprises one or more immunomodulatory polypeptides; and B) a second heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide, wherein the second heterodimer comprises one or more immunomodulatory polypeptides, and wherein the first heterodimer and the second heterodimer are covalently linked to one another. In some cases, the two TMMPs are identical to one another in amino acid sequence. In some cases, the first heterodimer and the second heterodimer are covalently linked to one another via a C-terminal region of the second polypeptide of the first heterodimer and a C-terminal region of the second polypeptide of the second heterodimer. In some cases, first heterodimer and the second heterodimer are covalently linked to one another via the C-terminal amino acid of the second polypeptide of the first heterodimer and the C-terminal region of the second polypeptide of the second

heterodimer; for example, in some cases, the C-terminal amino acid of the second polypeptide of the first heterodimer and the C-terminal region of the second polypeptide of the second heterodimer are linked to one another, either directly or via a linker. The linker can be a peptide linker. The peptide linker can have a length of from 1 amino acid to 200 amino acids (e.g., from 1 amino acid (aa) to 5 aa, from 5 aa to 10 aa, from 10 aa to 25 aa, from 25 aa to 50 aa, from 50 aa to 100 aa, from 100 aa to 150 aa, or from 150 aa to 200 aa). In some cases, the peptide epitope of the first heterodimer and the peptide epitope of the second heterodimer comprise the same amino acid sequence. In some cases, the first MHC polypeptide of the first and the second heterodimer is an MHC Class I β2-microglobulin, and wherein the second MHC polypeptide of the first and the second heterodimer is an MHC Class I heavy chain. In some cases, the immunomodulatory polypeptide of the first heterodimer and the immunomodulatory polypeptide of the second heterodimer comprise the same amino acid sequence. In some cases, the immunomodulatory polypeptide of the first heterodimer and the immunomodulatory polypeptide of the second heterodimer are variant immunomodulatory polypeptides that comprise from 1 to 10 amino acid substitutions compared to a corresponding parental wild-type immunomodulatory polypeptide, and wherein the from 1 to 10 amino acid substitutions result in reduced affinity binding of the variant immunomodulatory polypeptide to a cognate co-immunomodulatory polypeptide. In some cases, the immunomodulatory polypeptide of the first heterodimer and the immunomodulatory polypeptide of the second heterodimer are each independently selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1 (CD339), TGFβ, CD70, and ICAM. Examples, of suitable MHC polypeptides, immunomodulatory polypeptides, and peptide epitopes are described below.

MHC polypeptides

[0069] As noted above, a TMMP of the present disclosure includes MHC polypeptides. For the purposes of the instant disclosure, the term "major histocompatibility complex (MHC) polypeptides" is meant to include MHC polypeptides of various species, including human MHC (also referred to as human leukocyte antigen (HLA)) polypeptides, rodent (e.g., mouse, rat, etc.) MHC polypeptides, and MHC polypeptides of other mammalian species (e.g., lagomorphs, non-human primates, canines, felines, ungulates (e.g., equines, bovines, ovines, caprines, etc.), and the like. The term "MHC polypeptide" is meant to include Class I MHC polypeptides (e.g., β-2 microglobulin and MHC class I heavy chain).

[0070] In some cases, the first MHC polypeptide is an MHC Class I β2M (β2M) polypeptide, and the second MHC polypeptide is an MHC Class I heavy chain (H chain) ("MHC-H")). In other instances, the first MHC polypeptide is an MHC Class I heavy chain polypeptide; and the second MHC polypeptide is a β2M polypeptide. In some cases, both the β2M and MHC-H chain are of human origin; i.e., the MHC-H chain is an HLA heavy chain, or a variant thereof. Unless expressly stated otherwise, a TMMP of the present disclosure does not include membrane anchoring domains (transmembrane regions) of an MHC Class I heavy chain, or a part of MHC Class I heavy chain sufficient to anchor the

resulting TMMP to a cell (*e.g.*, eukaryotic cell such as a mammalian cell) in which it is expressed. In some cases, the MHC Class I heavy chain present in a TMMP of the present disclosure does not include a signal peptide, a transmembrane domain, or an intracellular domain (cytoplasmic tail) associated with a native MHC Class I heavy chain. Thus, e.g., in some cases, the MHC Class I heavy chain present in a TMMP of the present disclosure includes only the α1, α2, and α3 domains of an MHC Class I heavy chain. In some cases, the MHC Class I heavy chain present in a TMMP of the present disclosure has a length of from about 270 amino acids (aa) to about 290 aa. In some cases, the MHC Class I heavy chain present in a TMMP of the present disclosure has a length of 270 aa, 271 aa, 272 aa, 273 aa, 274 aa, 275 aa, 276 aa, 277 aa, 278 aa, 279 aa, 280 aa, 281 aa, 282 aa, 283 aa, 284 aa, 285 aa, 286 aa, 287 aa, 288 aa, 289 aa, or 290 aa.

[0071] In some cases, an MHC polypeptide of a TMMP is a human MHC polypeptide, where human MHC polypeptides are also referred to as "human leukocyte antigen" ("HLA") polypeptides. In some cases, an MHC polypeptide of a TMMP is a Class I HLA polypeptide, e.g., a β2-microglobulin polypeptide, or a Class I HLA heavy chain polypeptide. Class I HLA heavy chain polypeptides include HLA-A heavy chain polypeptides, HLA-B heavy chain polypeptides, HLA-C heavy chain polypeptides, HLA-E heavy chain polypeptides, HLA-F heavy chain polypeptides, and HLA-G heavy chain polypeptides.

MHC Class I heavy chains

[0072] In some cases, an MHC Class I heavy chain polypeptide present in a TMMP of the present disclosure comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of the amino acid sequence of any of the human HLA heavy chain polypeptides depicted in **FIGs. 7-13**. In some cases, the MHC Class I heavy chain has a length of 270 aa, 271 aa, 272 aa, 273 aa, 274 aa, 275 aa, 276 aa, 277 aa, 278 aa, 279 aa, 280 aa, 281 aa, 282 aa, 283 aa, 284 aa, 285 aa, 286 aa, 287 aa, 288 aa, 289 aa, or 290 aa. In some cases, an MHC Class I heavy chain polypeptide present in a TMMP of the present disclosure comprises 1-30, 1-5, 5-10, 10-15, 15-20, 20-25 or 25-30 amino acid insertions, deletions, and/or substitutions (in addition to those locations indicated as being variable in the heavy chain consensus sequences) of any one of the amino acid sequences depicted in **FIGs 7-13**. In some cases, the MHC Class I heavy chain does not include transmembrane or cytoplasmic domains. As an example, a MHC Class I heavy chain polypeptide of a TMMP of the present disclosure can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 25-300 (lacking all, or substantially all, of the leader, transmembrane and cytoplasmic sequence) or amino acids 25-365 (lacking the leader) of a human HLA-A heavy chain polypeptides depicted in any one of **FIG. 5A, 5B, and 5C**.

[0073] FIGs. 5A, 5B and 5C provide amino acid sequences of human leukocyte antigen (HLA) Class I heavy chain polypeptides. Signal sequences, amino acids 1-24, are bolded and underlined. FIG. 5A entry: 3A.1 is the HLA-A heavy chain (HLA-A*01:01:01:01 or A*0101) (NCBI accession NP_001229687.1), SEQ ID NO:23; entry 3A.2 is from HLA-A*1101 SEQ ID NO:24; entry 3A.3 is from HLA-A*2402 SEQ ID NO:25 and entry 3A.4 is from HLA-A*3303 SEQ ID NO:26. FIG. 5B provides the sequence HLA-B*07:02:01 (HLA-B*0702) NCBI GenBank Accession NP_005505.2 (see also GenBank Accession AUV50118.1.). FIG. 5C provides the sequence HLA- C*0701 (GenBank Accession NP_001229971.1) (HLA-C*07:01:01:01 or HLA-Cw*070101, HLA-Cw*07 see GenBank Accession CAO78194.1).

[0074] **FIG. 6** provides an alignment of eleven mature MHC class I heavy chain amino acid sequences without their leader sequences or transmembrane domains or intracellular domains. The aligned sequences are human HLA-A, HLA-B, and HLA-C, a mouse H2K protein sequence, three variants of HLA-A (var.1, var. 2C, and var.2CP), and 3 human HLA-A variants (HLA-A*1101; HLA-A*2402; and HLA-A*3303). Indicated in the alignment are the locations (84 and 139 of the mature proteins) where cysteine residues may be introduced (e.g., by substitution) for the formation of a disulfide bond to stabilize the MHC H chain - β2M complex. Also shown in the alignment is position 236 (of the mature polypeptide), which may be substituted by a cysteine residue that can form an inter-chain disulfide bond with β2M (*e.g.*, at aa 12). An arrow appears above each of those locations and the residues are bolded. The seventh HLA-A sequence shown in the alignment (var. 2c), shows the sequence of variant 2 substituted with C residues at positions 84, 139 and 236. The boxes flanking residues 84, 139 and 236 show the groups of five amino acids on either sides of those six sets of five residues, denoted aac1 (for "amino acid cluster 1"), aac2 (for "amino acid cluster 2"), aac3 (for "amino acid cluster 3"), aac4 (for "amino acid cluster 4"), aac5 (for "amino acid cluster 5"), and aac6 (for "amino acid cluster 6"), that may be replaced by 1 to 5 amino acids selected independently from (i) any naturally occurring amino acid or (ii) any naturally occurring amino acid except proline or glycine.

[0075] With regard to **FIG. 6**, in some cases: i) aac1 (amino acid cluster 1) may be the amino acid sequence GTLRG (SEQ ID NO:287) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, L replaced by I, V, A or F); ii) aac2 (amino acid cluster 2) may be the amino acid sequence YNQSE (SEQ ID NO:288) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by Q, Q replaced by N, and/or E replaced by D); iii) aac3 (amino acid cluster 3) may be the amino acid sequence TAADM (SEQ ID NO:289) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, T replaced by S, A replaced by G, D replaced by E, and/or M replaced by L, V, or I); iv) aac4 (amino acid cluster 4) may be the amino acid sequence AQTTK (SEQ ID NO:290) or that sequence with one or two amino acids deleted or substituted

with other naturally occurring amino acids (*e.g.*, A replaced by G, Q replaced by N, or T replaced by S, and/or K replaced by R or Q); v) aac5 (amino acid cluster 5) may be the amino acid sequence VETRP (SEQ ID NO:291) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, V replaced by I or L, E replaced by D, T replaced by S, and/or R replaced by K); and/or vi) aac6 (amino acid cluster 6) may be the amino acid sequence GDGTF (SEQ ID NO:292) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, D replaced by E, T replaced by S, or F replaced by L, W, or Y).

[0076] **FIGs. 7-9** provide alignments of mature HLA class I heavy chain amino acid sequences (without leader sequences or transmembrane domains or intracellular domains). The aligned amino acid sequences in **FIG. 7A** are HLA-A class I heavy chains of the following alleles: A*0101, A*0201, A*0301, A*1101, A*2301, A*2402, A*2407, A*3303, and A*3401. The aligned amino acid sequences in **FIG. 8A** are HLA-B class I heavy chains of the following alleles: B*0702, B*0801, B*1502, B*3802, B*4001, B*4601, and B*5301. The aligned amino acid sequences in **FIG. 9A** are HLA-C class I heavy chains of the following alleles: C*0102, C*0303, C*0304, C*0401, C*0602, C*0701, C*0801, and C*1502. Indicated in the alignments are the locations (84 and 139 of the mature proteins) where cysteine residues may be introduced (e.g., by substitution) for the formation of a disulfide bond to stabilize the HLA H chain - β2M complex. Also shown in the alignment is position 236 (of the mature polypeptide), which may be substituted by a cysteine residue that can form an inter-chain disulfide bond with β2M (*e.g.*, at aa 12). The boxes flanking residues 84, 139 and 236 show the groups of five amino acids on either sides of those six sets of five residues, denoted aac1 (for "amino acid cluster 1"), aac2 (for "amino acid cluster 2"), aac3 (for "amino acid cluster 3"), aac4 (for "amino acid cluster 4"), aac5 (for "amino acid cluster 5"), and aac6 (for "amino acid cluster 6"), that may be replaced by 1 to 5 amino acids selected independently from (i) any naturally occurring amino acid or (ii) any naturally occurring amino acid except proline or glycine.

[0077] **FIGs. 7A, 8A, and 9A** provide alignments of the amino acid sequences of mature HLA-A, -B, and -C class I heavy chains, respectively. The sequences are provided for the extracellular portion of the mature protein (without leader sequences or transmembrane domains or intracellular domains). As described in **FIG. 6**, the positions of aa residues 84, 139, and 236 and their flanking residues (aac1 to aac6) that may be replaced by 1 to 5 amino acids selected independently from (i) any naturally occurring amino acid or (ii) any naturally occurring amino acid except proline or glycine ae also shown. **FIG. 7B, 8B, and 9B** provide consensus amino acid sequences for the HLA-A, -B, and -C sequences, respectively, provide in FIG. 7A, 8A, and 9A. The consensus sequences show the variable amino acid positions as "X" residues sequentially numbered and the locations of amino acids 84, 139 and 236 double underlined.

[0078] With regard to **FIG. 7A**, in some cases: i) aac1 (amino acid cluster 1) may be the amino acid sequence GTLRG (SEQ ID NO:287) or that sequence with one or two amino acids deleted or

substituted with other naturally occurring amino acids (*e.g.*, L replaced by I, V, A or F); ii) aac2 (amino acid cluster 2) may be the amino acid sequence YNQSE (SEQ ID NO:288) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by Q, Q replaced by N, and/or E replaced by D); iii) aac3 (amino acid cluster 3) may be the amino acid sequence TAADM (SEQ ID NO:289) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, T replaced by S, A replaced by G, D replaced by E, and/or M replaced by L, V, or I); iv) aac4 (amino acid cluster 4) may be the amino acid sequence AQTTK (SEQ ID NO:290) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, A replaced by G, Q replaced by N, or T replaced by S, and or K replaced by R or Q); v) aac5 (amino acid cluster 5) may be the amino acid sequence VETRP (SEQ ID NO:291) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, V replaced by I or L, E replaced by D, T replaced by S, and/or R replaced by K); and/or vi) aac6 (amino acid cluster 6) may be the amino acid sequence GDGTF (SEQ ID NO:292) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, D replaced by E, T replaced by S, or F replaced by L, W, or Y).

[0079] With regard to **FIG. 8A**, in some cases: i) aac1 (amino acid cluster 1) may be the amino acid sequence RNLRG (SEQ ID NO:293) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by T or I; and/or L replaced by A; and/or the second R replaced by L; and/or the G replaced by R); ii) aac2 (amino acid cluster 2) may be the amino acid sequence YNQSE (SEQ ID NO:288) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by Q, Q replaced by N, and/or E replaced by D); iii) aac3 (amino acid cluster 3) may be the amino acid sequence TAADT (SEQ ID NO:294) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, the first T replaced by S; and/or A replaced by G; and/or D replaced by E; and/or the second T replaced by S); iv) aac4 (amino acid cluster 4) may be the amino acid sequence AQITQ (SEQ ID NO:295) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, A replaced by G; and/or the first Q replaced by N; and/or I replaced by L or V; and/or the T replaced by S; and/or the second Q replaced by N); v) aac5 (amino acid cluster 5) may be the amino acid sequence VETRP (SEQ ID NO:291) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, V replaced by I or L, E replaced by D, T replaced by S, and/or R replaced by K); and/or vi) aac6 (amino acid cluster 6) may be the amino acid sequence GDRTF (SEQ ID NO:296) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, D replaced by E; and/or T replaced by S; and/or R replaced by K or H; and/or F replaced by L, W, or Y).

[0080] With regard to **FIG. 9A**, in some cases: i) aac1 (amino acid cluster 1) may be the amino acid sequence RNLRG (SEQ ID NO:293) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by K; and/or L replaced by A or I; and/or the second R replaced by H; and/or the G replaced by T or S); ii) aac2 (amino acid cluster 2) may be the amino acid sequence YNQSE (SEQ ID NO:288) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, N replaced by Q, Q replaced by N, and/or E replaced by D); iii) aac3 (amino acid cluster 3) may be the amino acid sequence TAADT (SEQ ID NO:294) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, the first T replaced by S; and/or A replaced by G; and/or D replaced by E; and/or the second T replaced by S); iv) aac4 (amino acid cluster 4) may be the amino acid sequence AQITQ (SEQ ID NO:295) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, A replaced by G; and/or the first Q replaced by N; and/or I replaced by L; and/or the second Q replaced by N or K); v) aac5 (amino acid cluster 5) may be the amino acid sequence VETRP (SEQ ID NO:291) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, V replaced by I or L, E replaced by D, T replaced by S, and/or R replaced by K or H); and/or vi) aac6 (amino acid cluster 6) may be the amino acid sequence GDGTF (SEQ ID NO:292) or that sequence with one or two amino acids deleted or substituted with other naturally occurring amino acids (*e.g.*, D replaced by E; and/or T replaced by S; and/or F replaced by L, W, or Y).

HLA-A

[0081] In some cases, a TMMP of the present disclosure comprises an HLA-A heavy chain polypeptide. The HLA-A heavy chain peptide sequences, or portions thereof, that may be that may be incorporated into a TMMP of the present disclosure include, but are not limited to, the alleles: A*0101, A*0201, A*0301, A*1101, A*2301, A*2402, A*2407, A*3303, and A*3401, which are aligned without all, or substantially all, of the leader, transmembrane and cytoplasmic sequences in **FIG. 7A**. Any of those alleles may comprise a mutation at one or more of positions 84, 139 and/or 236 (as shown in **FIG. 7A**) selected from: a tyrosine to alanine at position 84 (Y84A); a tyrosine to cysteine at position 84 (Y84C); an alanine to cysteine at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In addition, HLA-A sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of the sequence of those HLA-A alleles may also be employed (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions).

[0082] In some cases, a TMMP of the present disclosure comprises an HLA-A heavy chain polypeptide comprising the following HLA-A consensus amino acid sequence:

[0083] GSHSMRYF**X1**TSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQ**X2**MEPRAPWIE QEGPEYWD**X3X4**T**X5X6X7**KA**X8**SQ**X9X10**R**X11X12**L**X13X14X15X16X17Y**YNQSE**X18**GSHT**X1 9**Q**X20**M**X21**GCDVG**X22**D**X23**RFLRGY**X24**Q**X25**AYDGKDYIAL**X26**EDLRSWTAADM**A**AQ**X27**T **X287X29**KWE**X30X31X32**EAEQ**X33**R**X34**YL**X35**G**X36**CV**X37X38**LRRYLENGKETLQRTD**X39**PK THMTHH**X40X41**SDHEATLRCWAL**X42**FYPAEITLTWQRDGEDQTQDTELVETRP**A**GDGTFQK WA**X43**VVVPSG**X44**EQRYTCHVQHEGLPKPLTLRWE**X45** (SEQ ID NO:29), wherein X1 is F, Y, S, or T; X2 is K or R; X3 is Q, G, E, or R; X4 is N or E; X5 is R or G; X6 is N or K; X7 is M or V; X8 is H or Q; X9 is T or I; X10 is D or H; X11 is A, V, or E; X12 is N or D; X13 is G or R; X14 is T or I; X15 is L or A; X16 is R or L; X17 is G or R; X18 is A or D; X19 is I, L, or V; X20 is I, R or M; X21 is F or Y; X22 is S or P; X23 is W or G; X24 is R, H, or Q; X25 is D or Y; X26 is N or K; X27 is T or I; X28 is K or Q; X29 is R or H; X30 is A or T; X31 is A or V; X32 is H or R; X33 is R, L, Q, or W; X34 is V or A; X35 is D or E; X36 is R or T; X37 is D or E; X38 is W or G; X39 is P or A; X40 is P or A; X41is V or I; X42 is S or G; X43 is A or S; X44 is Q or E; and X45 is P or L.

[0084] As one example, an MHC Class I heavy chain polypeptide of a TMMP can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A heavy chain amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:297).

[0085] In some cases, an HLA-A heavy chain polypeptide suitable for inclusion in a TMMP of the present disclosure comprises the following amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:297). This HLA-A heavy chain polypeptide is also referred to as "HLA-A*0201" or simply "HLA-A02." In some cases, the C-terminal Pro is not included in a TMMP of the present disclosure. For example, in some cases, an HLA-A02 polypeptide suitable for inclusion in a TMMP of the present disclosure comprises the following amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK

THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:461).

HLA-A (Y84A; A236C)

[0086] In some cases, the MHC Class I heavy chain polypeptide comprises Y84A and A236C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A heavy chain (Y84A; A236C) amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRG**A**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:298), where amino acid 84 is Ala and amino acid 236 is Cys. In some cases, the Cys-236 forms an interchain disulfide bond with Cys-12 of a variant β2M polypeptide that comprises an R12C substitution.

[0087] In some cases, an HLA-A heavy chain polypeptide suitable for inclusion in a TMMP of the present disclosure is an HLA-A02 (Y84A; A236C) polypeptide comprising the following amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRG**A**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:298).

[0088] In some cases, an HLA-A heavy chain polypeptide suitable for inclusion in a TMMP of the present disclosure is an HLA-A02 (Y84A; A236C) polypeptide comprising the following amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRG**A**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:462).

HLA-A (Y84C; A139C)

[0089] In some cases, the MHC Class I heavy chain polypeptide comprises Y84C and A139C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at

least 99%, or 100%, amino acid sequence identity to the following human HLA-A heavy chain (Y84C; A139C) amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET
RKVKAHSQTHRVDLGTLRG**C**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA
LKEDLRSWTAADM**C**AQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK
THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVV
VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:299), where amino acid 84 is Cys and amino acid 139 is Cys. In some cases, Cys-84 forms an intrachain disulfide bond with Cys-139.

HLA-A11 (HLA-A*1101)

[0090] As one non-limiting example, an MHC Class I heavy chain polypeptide of a TMMP can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A11 heavy chain amino acid sequence:
GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDQE
TRNVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDGKDYIA
LNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAYLEGTCVEWLRRYLENGKETLQRTDPPKT
HMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVVV
PSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:300). Such an MHC Class I heavy chain may be prominent in Asian populations, including populations of individuals of Asian descent.

HLA-A11 (Y84A; A236C)

[0091] As one non-limiting example, in some cases, the MHC Class I heavy chain polypeptide is an HLA-A11 allele that comprises Y84A and A236C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A A11 heavy chain (Y84A; A236C) amino acid sequence:
GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDQE
TRNVKAQSQTDRVDLGTLRG**A**YNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDGKDYIA
LNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAYLEGTCVEWLRRYLENGKETLQRTDPPKT
HMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVV
PSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:301), where amino acid 84 is Ala and amino acid 236 is Cys. In some cases, the Cys-236 forms an interchain disulfide bond with Cys-12 of a variant β2M polypeptide that comprises an R12C substitution.

HLA-A24 (HLA-A*2402)

[0092] As one non-limiting example, an MHC Class I heavy chain polypeptide of a TMMP of the present disclosure can comprise an amino acid sequence having at least 75%, at least 80%, at least

85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A24 heavy chain amino acid sequence:
GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDEET
GKVKAHSQTDRENLRIALRYYNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDGKDYIAL
KEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQRTDPPKT
HMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVVV
PSGEEQRYTCHVQHEGLPKPLTLRWEPSSQPTVPIVGIIAGLVLLGAVITGAVVAAVMWRRNSS
DRKGGSYSQAASSDSAQGSDVSLTACKV (SEQ ID NO:302). Such an MHC Class I heavy chain may be prominent in Asian populations, including populations of individuals of Asian descent. In some cases, amino acid 84 is an Ala. In some cases, amino acid 84 is a Cys. In some cases, amino acid 236 is a Cys. In some cases, amino acid 84 is an Ala and amino acid 236 is a Cys. In some cases, amino acid 84 is an Cys and amino acid 236 is a Cys.

HLA-A33 (HLA-A*3303)

[0093] As one non-limiting example, an MHC Class I heavy chain polypeptide of a TMMP of the present disclosure can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-A33 heavy chain amino acid sequence:
GSHSMRYFTTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDRN
TRNVKAHSQIDRVDLGTLRGYYNQSEAGSHTIQMMYGCDVGSDGRFLRGYQQDAYDGKDYIA
LNEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDPPKT
HMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWASVVV
PSGQEQRYTCHVQHEGLPKPLTLRWEPSSQPTIPIVGIIAGLVLFGAVFAGAVVAAVRWRRKSSD
RKGGSYSQAASSDSAQGSDMSLTACKV (SEQ ID NO:303). Such an MHC Class I heavy chain may be prominent in Asian populations, including populations of individuals of Asian descent. In some cases, amino acid 84 is an Ala. In some cases, amino acid 84 is a Cys. In some cases, amino acid 236 is a Cys. In some cases, amino acid 84 is an Ala and amino acid 236 is a Cys. In some cases, amino acid 84 is an Cys and amino acid 236 is a Cys.

HLA-B

[0094] In some cases, a TMMP of the present disclosure comprises an HLA-B heavy chain polypeptide. The HLA-B heavy chain peptide sequences, or portions thereof, that may be that may be incorporated into a TMMP of the present disclosure include, but are not limited to, the alleles: B*0702, B*0801, B*1502, B*3802, B*4001, B*4601, and B*5301, which are aligned without all, or substantially all, of the leader, transmembrane and cytoplasmic sequences in **FIG. 8A**. Any of those alleles may comprise a mutation at one or more of positions 84, 139 and/or 236 (as shown in **FIG. 8A**) selected from: a tyrosine to alanine at position 84 (Y84A); a tyrosine to cysteine at position 84 (Y84C); an alanine

to cysteine at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In addition, a HLA-B polypeptide comprising an amino acid sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of the sequence of those HLA-B alleles may also be employed (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions).

[0095] In some cases, a TMMP of the present disclosure comprises an HLA-B heavy chain polypeptide comprising the following HLA-B consensus amino acid sequence:

[0096] GSHSMRYF**X1**T**X2X3**SRPGRGEPRFI**X4**VGYVDDT**X5**FVRFDSDA**X6**SPR**X7X8**PR APWIEQEGPEYWDR**X9**TQ**X10X11**KT**X12X13**TQ**X14**Y**X15X16**NL**X17X18X19X20**YYNQSEAGS H**X21X22QX23**MYGCDLGPDGRLLRGHDQSAYDGKDYIALNEDL**X24**SWTAADTAAQI**X25**QRK **X26**EAAR**X27**AEQ**X28**R**X29**YLEG**X30**CVEWLRRYLENGK**X31X32**L**X33**RADPPKTHVTHHP**X34** SDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDRTFQKWAAVVVPSGEEQR YTCHVQHEGLPKPLTLRWEP (SEQ ID NO:30), wherein X1 is H, Y, or D; X2 is A or S; X3 is M or V; X4 is A, S, or T; X5 is Q or L; X6 is A or T; X7 is E, M K, or T; X8 is A or T; X9 is E or N; X10 is I or K; X11 is Y, F, S, or C; X12 is N or Q; X13 is A or T; X14 is D or Y; X15 is E or V; X16 is S or N; X17 is T, N, or I; X18 is A or L; X19 is L, or R; X20 is R or G; X21 is T or I; X22 is L or I; X23 is R or S; X24 is R or S; X25 is S or T; X26 is L or W; X27 is E OR V; X28 is R, D, L or W; X29 is A or T; X30 is L, E or T; X31 is E or D; X32 is K or T; X33 is E or Q; and X34 is I or V.

[0097] As an example, an MHC Class I heavy chain polypeptide of a TMMP of the present disclosure can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-B heavy chain amino acid sequence:

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYWDRNT QIYKAQAQTDRESLRNLRGYYNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDGKDYIAL NEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLERADPPKTH VTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDRTFQKWAAVVVPS GEEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:304).

HLA-B (Y84A; A236C)

[0098] As one non-limiting example, in some cases, the MHC Class I heavy chain polypeptide is an HLA-B polypeptide that comprises Y84A and A236C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-B heavy chain (Y84A; A236C) amino acid sequence:

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYWDRNT

QIYKAQAQTDRESLRNLRG**A**YNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDGKDYIAL NEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLERADPPKTH VTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQKWAAVVVPS GEEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:305), where amino acid 84 is Ala and amino acid 236 is Cys. In some cases, the Cys-236 forms an interchain disulfide bond with Cys-12 of a variant β2M polypeptide that comprises an R12C substitution.

HLA-B (Y84C; A139C)

[0099] In some cases, the MHC Class I heavy chain polypeptide comprises Y84C and A139C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-B heavy chain (Y84C; A139C) amino acid sequence:

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYWDRNT QIYKAQAQTDRESLRNLRG**C**YNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDGKDYIAL NEDLRSWTAADT**C**AQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLERADPPKTH VTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDRTFQKWAAVVVPS GEEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:306), where amino acid 84 is Cys and amino acid 139 is Cys. In some cases, Cys-84 forms an intrachain disulfide bond with Cys-139.

HLA-B*0702

[00100] As an example, in some cases, a MHC Class I heavy chain polypeptide present in a TMMP of the present disclosure comprises an amino acid sequence of HLA-B*0702 (SEQ ID NO:207) in **FIG. 8A**, or a sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100%, amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of that sequence (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions). In some cases, where the HLA-B heavy chain polypeptide of TMMP of the present disclosure has less than 100% identity to the sequence labeled HLA-B in **FIG. 6**, or labeled "B*0702 in **FIG. 8A**, it may comprise a mutation at one or more of positions 84, 139 and/or 236 selected from: a tyrosine to alanine substitution at position 84 (Y84A); a tyrosine to cysteine substitution at position 84 (Y84C); an alanine to cysteine at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In some cases, the HLA-B heavy chain polypeptide of TMMP of the present disclosure comprises Y84A and A236C substitutions. In some cases, the HLA-B*0702 heavy chain polypeptide of TMMP of the present disclosure comprises Y84C and A139C substitutions. In some cases, the HLA-B heavy chain polypeptide of TMMP of the present disclosure comprises Y84C, A139C, and A236C substitutions.

HLA-C

[00101] In some cases, a TMMP of the present disclosure comprises an HLA-C heavy chain polypeptide. The HLA-C heavy chain polypeptide, or portions thereof, that may be that may be incorporated into a TMMP of the present disclosure include, but are not limited to, the alleles: C*0102, C*0303, C*0304, C*0401, C*0602, C*0701, C*0801, and C*1502, which are aligned without all, or substantially all, of the leader, transmembrane and cytoplasmic sequences in **FIG. 9A**. Any of those alleles may comprise a mutation at one or more of positions 84, 139 and/or 236 (as shown in **FIG. 9A**) selected from: a tyrosine to alanine substitution at position 84 (Y84A); a tyrosine to cysteine substitution at position 84 (Y84C); an alanine to cysteine substitution at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In addition, an HLA-C polypeptide comprising an amino acid sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of the sequence of those HLA-C alleles may also be employed (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions).

[00102] In some cases, a TMMP of the present disclosure comprises an HLA-C heavy chain polypeptide comprising the following HLA-C consensus amino acid sequence:

[00103] **X1**SHSM**X2**YF**X3**TAVS**X4**PGRGEP**X5**FI**X6**VGYVDDTQFV**X7**FDSDAASPRGEPR**X8**PWVEQEGPEYWDRETQ**X9**YKRQAQ**X10**DRV**X11**LR**X12**LRGYYNQSE**X13X14**SH**X15X16**Q**X17**M**X18**GCD**X19**GPDGRLLRG**X20X21**Q**X22**AYDGKDYIALNEDLRSWTAADTAAQITQRK**X23**EAAR**X24**AEQ**X25**RAYLEG**X26**CVEWLRRYL**X27**NGK**X28**TLQRAE**X29**PKTHVTHHP**X30**SDHEATLRCWALGFYPAEITLTWQ**X31**DGEDQTQDTELVETRPAGDGTFQKWAAV**X32**VPS**GX33**EQRYTCH**X34**QHEGL**X35**EPLTL**X36**W**X37**P (SEQ ID NO:31), wherein X1 is C or G; X2 is R or K; X3 is F, Y, S, or D; X4 is R or W; X5 is H or R; X6 is A or S; X7 is Q or R; X8 is A or E; X9 is N or K;X10 is T or A; X11 is S or N; X12 is N or K; X13 is A or D; X14 is G or R; X15 is T or I; X16 is L or I; X17 is W or R; X18 is C, Y, F, or S; X19 is L, or V; X20 is Y or H; X21 is D or N; X22 is Y, F, S, or L; X23 is L or W; X24 is E, A, Or T; X25 is R, L, or W; X26 is L or T; X27 is E OR K; X28 is E or K; X29 is H or P; X30 is R or V; X31 is W or R; X32 is V or M; X33 is E or Q; X34 is M or V; X35 is P or Q; X36 is R or S; and X37 is P or G.

[00104] As an example, an MHC Class I heavy chain polypeptide of a TMMP of the present disclosure can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-C heavy chain amino acid sequence:

CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYWDRETQNYKRQAQADRVSLRNLRGYYNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQSAYDGKDYI

ALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKETLQRAEPPKT
HVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVVV
PSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:307).

HLA-C (Y84A; A236C)

[00105] As one non-limiting example, in some cases, the MHC Class I heavy chain polypeptide is an HLA-C polypeptide that comprises Y84A and A236C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-C heavy chain (Y84A; A236C) amino acid sequence:
CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYWDRE
TQNYKRQAQADRVSLRNLRG**A**YNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQSAYDGKDYI
ALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKETLQRAEPPKT
HVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVV
PSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:308), where amino acid 84 is Ala and amino acid 236 is Cys. In some cases, the Cys-236 forms an interchain disulfide bond with Cys-12 of a variant β2M polypeptide that comprises an R12C substitution.

HLA-C (Y84C; A139C)

[00106] In some cases, the MHC Class I heavy chain polypeptide comprises Y84C and A139C substitutions. For example, in some cases, the MHC Class I heavy chain polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following human HLA-C heavy chain (Y84C; A139C) amino acid sequence:
CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYWDRE
TQNYKRQAQADRVSLRNLRG**C**YNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQSAYDGKDYI
ALNEDLRSWTAADT**C**AQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKETLQRAEPPKT
HVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTFQKWAAVVV
PSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:397), where amino acid 84 is Cys and amino acid 139 is Cys. In some cases, Cys-84 forms an intrachain disulfide bond with Cys-139.

HLA-C*0701

[00107] In some cases, a MHC Class I heavy chain polypeptide of a TMMP of the present disclosure comprises an amino acid sequence of HLA-C*0701 of **FIG. 9A** (labeled HLA-C in **FIG. 6**), or an amino acid sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of that sequence (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions). In some cases, where the

HLA-C heavy chain polypeptide of a TMMP of the present disclosure has less than 100% identity to the sequence labeled HLA-C*0701 in **FIG. 9A**, it may comprise a mutation at one or more of positions 84, 139 and/or 236 selected from: a tyrosine to alanine substitution at position 84 (Y84A); a tyrosine to cysteine substitution at position 84 (Y84C); an alanine to cysteine at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In some cases, the HLA-C heavy chain polypeptide of a TMMP of the present disclosure comprises Y84A and A236C substitutions. In some cases, the HLA-C*0701 heavy chain polypeptide of a T-Cell-MMP or its epitope conjugate comprises Y84C and A139C substitutions. In some cases, the HLA-C heavy chain polypeptide of a TMMP of the present disclosure comprises Y84C, A139C, and A236C substitutions.

Non-classical HLA-E, -F, and -G MHC Class I heavy chains

[00108] In some cases, a TMMP of the present disclosure comprises a non-classical MHC Class I heavy chain polypeptide. Among the non-classical HLA heavy chain polypeptides, or portions thereof, that may be that may be incorporated into a TMMP of the present disclosure include, but are not limited to, those of HLA-E, -F, and -G alleles. Amino acid sequences for HLA-E, -F, and -G heavy chain polypeptides, (and the HLA-A, B and C alleles) may be found on the world wide web hla.alleles.org/ nomenclature/index.html, the European Bioinformatics Institute (www(dot)ebi(dot)ac(dot)uk), which is part of the European Molecular Biology Laboratory(EMBL), and at the National Center for Biotechnology Information (www(dot)ncbi(dot)nlm(dot)nih(dot)gov).

[00109] Non-limiting examples of suitable HLA-E alleles include, but are not limited to, HLA-E*0101 (HLA-E*01:01:01:01), HLA-E*01:03(HLA-E*01:03:01:01), HLA-E*01:04, HLA-E*01:05, HLA-E*01:06, HLA-E*01:07, HLA-E*01:09, and HLA-E*01:10. Non-limiting examples of suitable HLA-F alleles include, but are not limited to, HLA-F*0101 (HLA-F*01:01:01:01), HLA-F*01:02, HLA-F*01:03(HLA-F*01:03:01:01), HLA-F*01:04, HLA-F*01:05, and HLA-F*01:06. Non-limiting examples of suitable HLA-G alleles include, but are not limited to, HLA-G*0101 (HLA-G*01:01:01:01), HLA-G*01:02, HLA-G*01:03(HLA-G*01:03:01:01), HLA-G*01:04 (HLA-G*01:04:01:01), HLA-G*01:06, HLA-G*01:07, HLA-G*01:08, HLA-G*01:09: HLA-G*01:10, HLA-G*01:10, HLA-G*01:11, HLA-G*01:12, HLA-G*01:14, HLA-G*01:15, HLA-G*01:16, HLA-G*01:17, HLA-G*01:18: HLA-G*01:19, HLA-G*01:20, and HLA-G*01:22. Consensus sequences for those HLA E, -F and -G alleles without all, or substantially all, of the leader, transmembrane and cytoplasmic sequences are provided in **FIG. 10**, and aligned with consensus sequences of the above-mentioned HLA-A, -B and -C alleles in **FIG. 11**.

[00110] **FIG. 1-** provides a consensus sequence for each of HLA-E, -F, and -G with the variable aa positions indicated as "X" residues sequentially numbered and the locations of aas 84, 139 and 236 double underlined.

[00111] **FIG. 11** provides an alignment of the consensus amino acid sequences for HLA-A, -B, -C, -E, -F, and -G, which are given in FIGs. 7-11. Variable residues in each sequence are listed as "X" with the sequential numbering removed. As indicated in FIG. 6, the locations of aas 84, 139 and 236 are indicated with their flanking five-amino acid clusters that may be replaced by 1 to 5 amino acids selected independently from (i) any naturally occurring amino acid or (ii) any naturally occurring amino acid except proline or glycine are also shown.

[00112] Any of the above-mentioned HLA-E, -F, and/or -G alleles may comprise a substitution at one or more of positions 84, 139 and/or 236 as shown in **FIG. 11** for the consensus sequences. In some cases, the substitutions may be selected from a: position 84 tyrosine to alanine (Y84A) or cysteine (Y84C), or, in the case of HLA-F, an R84A or R84C substitution; a position 139 alanine to cysteine (A139C), or, in the case of HLA-F, a V139C; and an alanine to cysteine substitution at position 236 (A236C). In addition, an HLA-E, -F and /or -G sequence having at least 75% (e.g., at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%) or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of any of the consensus sequences of set forth in **FIG. 11** may also be employed (*e.g.,* the sequences may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions in addition to changes at variable residues listed therein).

Mouse H2K

[00113] In some cases, a MHC Class I heavy chain polypeptide present in a TMMP of the present disclosure comprises an amino acid sequence of MOUSE H2K (SEQ ID NO:45) (MOUSE H2K in **FIG. 6**), or a sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to all or part (e.g., 50, 75, 100, 150, 200, or 250 contiguous amino acids) of that sequence (*e.g.,* it may comprise 1-25, 1-5, 5-10, 10-15, 15-20, 20-25, or 25-30 amino acid insertions, deletions, and/or substitutions). In some cases, where the MOUSE H2K heavy chain polypeptide of a TMMP of the present disclosure has less than 100% identity to the sequence labeled MOUSE H2K in **FIG. 6**, it may comprise a mutation at one or more of positions 84, 139 and/or 236 selected from: a tyrosine to alanine at position 84 (Y84A); a tyrosine to cysteine at position 84 (Y84C); an alanine to cysteine at position 139 (A139C); and an alanine to cysteine substitution at position 236 (A236C). In some cases, the MOUSE H2K heavy chain polypeptide of a TMMP of the present disclosure comprises Y84A and A236C substitutions. In some cases, the MOUSE H2K heavy chain polypeptide of a TMMP of the present disclosure comprises Y84C and A139C substitutions. In some cases, the MOUSE H2K heavy chain polypeptide of a TMMP of the present disclosure comprises Y84C, A139C and A236C substitutions.

Exemplary combinations

[00114] Table 1, below, presents various combinations of MHC Class I heavy chain sequence modifications that can be incorporated in a TMMP of the present disclosure.

TABLE 1

Entry	HLA Heavy Chain Sequence	Sequence Identity Range‡	Specific Substitutions at aa positions 84, 139 and/or 236
1	HLA-A Consensus (**FIG. 7B**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions (not counting variable residues)	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
2	A*0101, A*0201, A*0301, A*1101, A*2402, A*2301, A*2402, A*2407, A*3303, or A*3401 (**FIG. 7A**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
3	HLA-B Consensus (**FIG. 8B**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions (not counting variable residues)	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
4	B*0702, B*0801, B*1502, B*3802, B*4001, B*4601, or B*5301 (**FIG. 8A**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
5	HLA-C Consensus (**FIG. 9B**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions (not counting variable residues)	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)

Entry	HLA Heavy Chain Sequence	Sequence Identity Range‡‡	Specific Substitutions at aa positions 84, 139 and/or 236
6	C*0102, C*0303, C*0304, C*0401, C*0602, C*0701, C*0801, or C*1502 (**FIG. 9A**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
7	HLA-E, F, or G Consensus (**FIG. 10**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions (not counting variable residues)	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)
8	MOUSE H2K (**FIG. 6**)	75%-99.8%, 80%-99.8%, 85%-99.8%, 90%-99.8%, 95%-99.8%, 98%-99.8%, or 99%-99.8%; or 1-25, 1-5, 5-10, 10-15, 15-20, or 20-25 aa insertions, deletions, and/or substitutions	None; Y84C; Y84A; A139C; A236C; (Y84A & A236C); (Y84C & A139C); or (Y84C, A139C & A236C)

‡‡ The Sequence Identity Range is the permissible range in sequence identity of a MHC-H polypeptide sequence incorporated into a TMMP relative to the corresponding portion of the sequences listed in FIG. 6-11 not counting the variable residues in the consensus sequences.

Beta-2 microglobulin

[00115] A β2-microglobulin (β2M) polypeptide of a TMMP of the present disclosure can be a human β2M polypeptide, a non-human primate β2M polypeptide, a murine β2M polypeptide, and the like. In some instances, a β2M polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a β2M amino acid sequence depicted in FIG. 6. In some instances, a β2M polypeptide comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 21 to 119 of a β2M amino acid sequence depicted in FIG. 4.

[00116] In some cases, a suitable β2M polypeptide comprises the following amino acid sequence:

[00117] IQRTPKIQVY SCHPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTLSQP KIVKWDRDM (SEQ ID NO:311); and the HLA Class I heavy chain polypeptide comprises the following amino acid sequence:

[00118] GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE GPEYWDGETRKVKAHSQTHRVDL(aa1){C}(aa2)AGSHTVQRMYGCDVGSDWRFLRGYHQYAY

DGKDYIALKEDLRSW(aa3){C}(aa4))HKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQR TDAPKTHMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTEL(aa5)(C)(aa6)QKWAA VVVPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:309), where the cysteine residues indicated as {C} form an disulfide bond between the α1 and α2-1 helices and the (C) residue forms a disulfide bond with the β2M polypeptide cysteine at position 12. In the sequence above, "aa1" is "amino acid cluster 1" ; "aa2" is "amino acid cluster 2"; "aa3" is "amino acid cluster 3" ; "aa4" is "amino acid cluster 4" ; "aa5" is "amino acid cluster 5"; and "aa6" is "amino acid cluster 6"; see, e.g., FIG. 8. Each occurrence of aa1, aa2, aa3, aa4, aa5, and aa6 is and independently selected to be 1-5 amino acid residues, wherein the amino acid residues are i) selected independently from any naturally occurring (e.g., encoded) amino acid or ii) any naturally occurring amino acid except proline or glycine.

[00119] In some cases, an MHC polypeptide comprises a single amino acid substitution relative to a reference MHC polypeptide (where a reference MHC polypeptide can be a wild-type MHC polypeptide), where the single amino acid substitution substitutes an amino acid with a cysteine (Cys) residue. Such cysteine residues, when present in an MHC polypeptide of a first polypeptide of a TMMP of the present disclosure, can form a disulfide bond with a cysteine residue present in a second polypeptide chain of a TMMP of the present disclosure.

[00120] In some cases, a first MHC polypeptide in a first polypeptide of a TMMP of the present disclosure, and/or the second MHC polypeptide in the second polypeptide of a TMMP of the present disclosure, includes an amino acid substitution to substitute an amino acid with a cysteine, where the substituted cysteine in the first MHC polypeptide forms a disulfide bond with a cysteine in the second MHC polypeptide, where a cysteine in the first MHC polypeptide forms a disulfide bond with the substituted cysteine in the second MHC polypeptide, or where the substituted cysteine in the first MHC polypeptide forms a disulfide bond with the substituted cysteine in the second MHC polypeptide.

[00121] For example, in some cases, one of following pairs of residues in an HLA β2-microglobulin and an HLA Class I heavy chain is substituted with cysteines (where residue numbers are those of the mature polypeptide): 1) β2M residue 12, HLA Class I heavy chain residue 236; 2) β2M residue 12, HLA Class I heavy chain residue 237; 3) β2M residue 8, HLA Class I heavy chain residue 234; 4) β2M residue 10, HLA Class I heavy chain residue 235; 5) β2M residue 24, HLA Class I heavy chain residue 236; 6) β2M residue 28, HLA Class I heavy chain residue 232; 7) β2M residue 98, HLA Class I heavy chain residue 192; 8) β2M residue 99, HLA Class I heavy chain residue 234; 9) β2M residue 3, HLA Class I heavy chain residue 120; 10) β2M residue 31, HLA Class I heavy chain residue 96; 11) β2M residue 53, HLA Class I heavy chain residue 35; 12) β2M residue 60, HLA Class I heavy chain residue 96; 13) β2M residue 60, HLA Class I heavy chain residue 122; 14) β2M residue 63, HLA Class I heavy chain residue 27; 15) β2M residue Arg3, HLA Class I heavy chain residue Gly120; 16) β2M residue His31, HLA Class I heavy chain residue Gln96; 17) β2M residue Asp53, HLA Class I

heavy chain residue Arg35; 18) β2M residue Trp60, HLA Class I heavy chain residue Gln96; 19) β2M residue Trp60, HLA Class I heavy chain residue Asp122; 20) β2M residue Tyr63, HLA Class I heavy chain residue Tyr27; 21) β2M residue Lys6, HLA Class I heavy chain residue Glu232; 22) β2M residue Gln8, HLA Class I heavy chain residue Arg234; 23) β2M residue Tyr10, HLA Class I heavy chain residue Pro235; 24) β2M residue Ser11, HLA Class I heavy chain residue Gln242; 25) β2M residue Asn24, HLA Class I heavy chain residue Ala236; 26) β2M residue Ser28, HLA Class I heavy chain residue Glu232; 27) β2M residue Asp98, HLA Class I heavy chain residue His192; and 28) β2M residue Met99, HLA Class I heavy chain residue Arg234. The amino acid numbering of the MHC/HLA Class I heavy chain is in reference to the mature MHC/HLA Class I heavy chain, without a signal peptide. For example, in some cases, residue 236 of the mature HLA-A amino acid sequence is substituted with a Cys. In some cases, residue 236 of the mature HLA-B amino acid sequence is substituted with a Cys. In some cases, residue 236 of the mature HLA-C amino acid sequence is substituted with a Cys. In some cases, residue 32 (corresponding to Arg-12 of mature β2M) of an amino acid sequence depicted in FIG. 4 is substituted with a Cys.

[00122] In some cases, a β2M polypeptide comprises the amino acid sequence: IQRTPKIQVY S**R**HPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTLSQP KIVKWDRDM (SEQ ID NO:310). In some cases, a β2M polypeptide comprises the amino acid sequence: IQRTPKIQVY S**C**HPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTLSQP KIVKWDRDM (SEQ ID NO:311).

[00123] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**A**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:297).

[00124] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:312).

[00125] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:
GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET
RKVKAHSQTHRVDLGTLRG**A**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA
LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK
THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV
VPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:313).

[00126] In some cases, the β2M polypeptide comprises the following amino acid sequence:

[00127] IQRTPKIQVY S**C**HPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTLSQP KIVKWDRDM (SEQ ID NO:311); and the HLA Class I heavy chain polypeptide of a TMMP of the present disclosure comprises the following amino acid sequence:

[00128] GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE GPEYWDGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQY AYDGKDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKE TLQRTDAPKTHMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGT FQKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:312), where the Cys residues that are underlined and in bold form a disulfide bond with one another in the TMMP.

[00129] In some cases, the β2M polypeptide comprises the amino acid sequence:
IQRTPKIQVYS**C**HPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSFYLL
YYTEFTPTEKDEYACRVNHVTLSQPKIVKWDRDM (SEQ ID NO:314).

[00130] In some cases, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are disulfide linked to one another through: i) a Cys residue present in a linker connecting the peptide epitope and a β2M polypeptide in the first polypeptide chain; and ii) a Cys residue present in an MHC Class I heavy chain in the second polypeptide chain. In some cases, the Cys residue present in the MHC Class I heavy chain is a Cys introduce as a Y84C substitution. In some cases, the linker connecting the peptide epitope and the β2M polypeptide in the first polypeptide chain is GCGGS(G4S)n (SEQ ID NO:315), where n is 1, 2, 3, 4, 5, 6, 7, 8, or 9. For example, in some cases, the linker comprises the amino acid sequence GCGGSGGGGSGGGGSGGGGS (SEQ ID NO:316). As another example, the linker comprises the amino acid sequence GCGGSGGGGSGGGGS (SEQ ID NO:317). Examples of disulfide-linked first and second polypeptides of a TMMP of the present disclosure are depicted schematically in FIG. 2A-2F.

Multiple disulfide bonded TMMPs

[00131] In some cases, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are linked to one another by at least two disulfide bonds (i.e., two interchain disulfide bonds). Examples of such multiple disulfide-linked TMMP are depicted schematically in FIG. 12A and 12B and FIG. 13A-13C. In addition, where a TMMP of the present disclosure comprises an IgFc polypeptide, a heterodimeric TMMP can be dimerized, such that disulfide bonds link the IgFc polypeptides in the two heterodimeric TMMPs. Such an arrangement is depicted schematically in FIG. 12C and 12D, where disulfide bonds are represented by dashed lines. Unless otherwise stated, the at least two disulfide bonds described in the multiple disulfide-linked TMMPPs in this section are not referring to disulfide bonds linking IgFc polypeptides in dimerized TMMPs.

[00132] As noted above, in some cases, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are linked to one another by at least two disulfide bonds (i.e., two interchain disulfide bonds). For example, in some instances, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are linked to one another by 2 interchain disulfide bonds. As another example, in some instances, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are linked to one another by 3 interchain disulfide bonds. As another example, in some instances, the first polypeptide and the second polypeptide of a TMMP of the present disclosure are linked to one another by 4 interchain disulfide bonds.

[00133] In some cases where a peptide epitope in a first polypeptide of a TMMP of the present disclosure is linked to a β2M polypeptide by a linker comprising a Cys, at least one of the at least two disulfide bonds links a Cys in the linker to a Cys in an MHC Class I heavy chain in the second polypeptide. In some cases, where a peptide epitope in a first polypeptide of a TMMP of the present disclosure is linked to an MHC Class I heavy chain polypeptide by a linker, at least one of the at least two disulfide bonds links a Cys in the linker to a Cys in a β2M polypeptide present in the second polypeptide.

[00134] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) exhibits increased stability, compared to a control TMMP that includes only one of the at least two disulfide bonds. In some cases, a multiple disulfide-linked TMMP (e.g., a double disulfide-linked TMMP) of the present disclosure exhibits increased *in vitro* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds. For example, in some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) exhibits at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold, greater *in vitro* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds.

[00135] Whether a multiple disulfide-linked TMMP of the present disclosure exhibits increased *in vitro* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds, can be determined by measuring the amount disulfide-linked heterodimeric TMMP present in a sample over time and/or under a specified condition and/or during purification of the TMMP.

[00136] For example, in some cases, a multiple disulfide-linked TMMP (e.g., a double disulfide-linked TMMP) of the present disclosure exhibits at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold, greater *in vitro* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds, when the TMMP is stored at 37°C for a period of time (e.g., for a period of time of from about 1 week to about 2 weeks, from about 2 weeks to about 4 weeks, or from about 4 weeks to about 2 months). For example, in some cases, the amount of disulfide-linked heterodimeric TMMP remaining after storing a multiple disulfide-linked TMMP (e.g., a double disulfide-linked TMMP) of the present disclosure *in vitro* at 37°C for 28 days is at least at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold, greater than the amount of disulfide-linked heterodimeric TMMP remaining after storing a control TMMP (a TMMP that includes only one of the at least two disulfide bonds present in the multiple disulfide-linked TMMP) *in vitro* at 37°C for 28 days.

[00137] In some cases, a multiple disulfide-linked TMMP of the present disclosure exhibits increased *in vivo* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds. For example, in some cases, a multiple disulfide-linked TMMP of the present disclosure exhibits at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold, greater *in vivo* stability, compared to a control TMMP that includes only one of the at least two disulfide bonds.

[00138] In some cases, the presence of two disulfide bonds in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) provides for increased production of disulfide-linked heterodimeric TMMP, compared to the amount of disulfide-linked heterodimeric TMMP produced when the TMMP is a control TMMP that includes only one of the at least two disulfide bonds. For example, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) can be produced in a mammalian cell in *in vitro* cell culture, where the mammalian cell is cultured in a liquid cell culture medium. The TMMP can be secreted into the cell culture medium. The cells can be lysed, generating a cell lysate, and the TMMP can be present in the cell lysate. The TMMP can be purified from the cell culture medium and/or the cell lysate. For example, where the TMMP comprises an IgG1 Fc polypeptide, the cell culture medium and/or the cell lysate can be contacted with immobilized protein A (e.g., the cell culture medium and/or the cell lysate can be applied to a protein A column, where protein A is immobilized onto beads). TMMP present in the cell culture medium and/or the cell lysate becomes bound to the immobilized protein A. After washing the column to remove

unbound materials, the bound TMMP is eluted, generating a protein A eluate. The amount of disulfide-linked heterodimeric TMMP present in the protein A eluate is a least 0.5%, at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, or at least 10%, higher than the amount of disulfide-linked heterodimeric TMMP present in the protein A eluate when the TMMP is a control TMMP that includes only one of the at least two disulfide bonds present in the multiple disulfide-linked TMMP (e.g., a double disulfide-linked TMMP). In some cases, the percent of the total TMMP protein in the eluate that is non-aggregated disulfide-linked heterodimeric TMMP is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99%. The protein A eluate can be subjected to size exclusion chromatography (SEC) and/or one or more other additional purification steps.

[00139] In some cases, a T-cell modulatory multimeric polypeptide of the present disclosure comprises at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope, where the peptide has a length of at least 4 amino acids (e.g., from 4 amino acids to 25 amino acids; e.g., the peptide has a length of 4, 5, 6, 7, 8, 9, 10-15, 15-20, or 20-25 amino acids); and ii) first MHC polypeptide; b) a second polypeptide comprising a second MHC polypeptide, and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the immunomodulatory polypeptide, and where the heterodimer comprises at least two disulfide bonds (e.g., two disulfide bonds) between the first polypeptide and the second polypeptide (e.g., the heterodimer comprises: i) a first disulfide bond linking the first polypeptide and the second polypeptide; and ii) a second disulfide bond linking the first polypeptide and the second polypeptide). Expressed another way, the first polypeptide comprises a first Cys residue that forms a disulfide bond (a first disulfide bond) with a first Cys residue in the second polypeptide; and the first polypeptide comprises a second Cys residue that forms a disulfide bond (a second disulfide bond) with a second Cys residue in the second polypeptide.

[00140] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a peptide linker; and iii) a β2M polypeptide; and b) a second polypeptide comprising an MHC Class I heavy chain polypeptide, where one or both of the first and the second polypeptides comprises at least one immunomodulatory polypeptide, where the TMMP comprises: a) a first disulfide linkage between: i) a Cys present in the linker between the peptide epitope and the β2M polypeptide; and ii) a first Cys introduced into the MHC Class I heavy chain polypeptide; and b) at least a second disulfide linkage between the first polypeptide and the second polypeptide, where the at least a second disulfide linkage is between: i) a Cys in the first polypeptide that is C-terminal to the Cys present in the linker; and ii) a Cys in the second polypeptide that is C-terminal to the first Cys introduced into the MHC Class I heavy chain polypeptide.

[00141] In some cases, a first and a second disulfide bond-forming Cys residues in a first or a second polypeptide of a TMMP of the present disclosure are from about 10 amino acids to about 200 amino acids apart from one another. For example, in some cases, a first and a second disulfide bond-forming Cys residues in a first or a second polypeptide of a TMMP are from about 10 amino acids (aa) to about 15 aa, from about 15 aa to about 20 aa, from about 20 aa to about 25 aa, from about 25 aa to about 30 aa, from about 30 aa to about 40 aa, from about 40 aa to about 50 aa, from about 50 aa to about 60 aa, from about 60 aa to about 70 aa, from about 70 aa to about 80 aa, from about 80 aa to about 90 aa, from about 90 aa to about 100 aa, from about 100 aa to about 110 aa, from about 110 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, from about 150 aa to about 160 aa, from about 160 aa to about 170 aa, from about 170 aa to about 180 aa, from about 180 aa to about 190 aa, or from about 190 aa to about 200 aa.

[00142] As an example, in some cases, the first and second disulfide bond-forming Cys residues in the first polypeptide of a TMMP of the present disclosure are from about 10 amino acids to about 80 amino acid residues apart from one another. For example, in some cases, the second disulfide bond-forming Cys residue in the first polypeptide is from about 10 amino acids to about 80 amino acids (e.g., from about 10 amino acids (aa) to about 15 aa, from about 15 aa to about 20 aa, from about 20 aa to about 25 aa, from about 25 aa to about 30 aa, from about 30 aa to about 40 aa, from about 40 aa to about 50 aa, from about 50 aa to about 60 aa, from about 60 aa to about 70 aa, or from about 70 aa to about 80 aa) C-terminal to the first disulfide bond-forming Cys residue in the first polypeptide. In some cases, the second disulfide bond-forming Cys residue in the first polypeptide is 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, 20 aa, 21 aa, 22 aa, 23 aa, 24 aa, or 25 aa, C-terminal to the first disulfide bond-forming Cys residue in the first polypeptide. In some cases, the second disulfide bond-forming Cys residue in the first polypeptide is 15 aa C-terminal to the first disulfide bond-forming Cys residue in the first polypeptide. In some cases, the second disulfide bond-forming Cys residue in the first polypeptide is 20 aa C-terminal to the first disulfide bond-forming Cys residue in the first polypeptide. In some cases, the second disulfide bond-forming Cys residue in the first polypeptide is 25 aa C-terminal to the first disulfide bond-forming Cys residue in the first polypeptide.

[00143] As another example, in some cases, the first and second disulfide bond-forming Cys residues in the second polypeptide of a TMMP of the present disclosure are from about 140 amino acids to about 160 amino acids apart from one another. For example, in some cases, the second disulfide bond-forming Cys residue in the second polypeptide is from about 140 amino acids to about 160 amino acids C-terminal to the first disulfide bond-forming Cys residue in the second polypeptide. In some cases, the second disulfide bond-forming Cys residue in the second polypeptide is 140 amino acids (aa), 141 aa, 142 aa, 143 aa, 144 aa, 145 aa, 146 aa, 147 aa, 148 aa, 149 aa, 150 aa, 151 aa, 152 aa, 153 aa, 154 aa,

155 aa, 156 aa, 157 aa, 158 aa, 159 aa, or 160 aa, C-terminal to the first disulfide bond-forming Cys residue in the second polypeptide.

[00144] A multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) can comprise, for example: a) a first polypeptide comprising: i) a peptide epitope (e.g., a peptide of from 4 amino acids to about 25 amino acids that is bound by a TCR when the peptide is complexed with MHC polypeptides); and ii) a first MHC polypeptide, where the first polypeptide comprises a peptide linker between the peptide and the first MHC polypeptide, where the peptide linker comprises a Cys residue, and where the first MHC polypeptide is a β2M polypeptide that comprises an amino acid substitution that introduces a Cys residue; b) and a second polypeptide comprising a second MHC polypeptide, where the second MHC polypeptide is a Class I heavy chain comprising a Y84C substitution and an A236C substitution, based on the amino acid numbering of HLA-A*0201 (depicted in FIG. 7A), or at corresponding positions in another Class I heavy chain allele, where the TMMP comprises a disulfide bond between the Cys residue in the peptide linker and the Cys residue at amino acid position 84 of the Class I heavy chain or corresponding position of another Class I heavy chain allele, and where the TMMP comprises a disulfide bond between the introduced Cys residue in the β2M polypeptide and the Cys at amino acid position 236 of the Class I heavy chain or corresponding position of another Class I heavy chain allele; and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the at least one immunomodulatory polypeptide. Examples are depicted schematically in FIG. 12A and FIG. 12B.

[00145] In some cases, the peptide linker comprises the amino acid sequence GCGGS (SEQ ID NO:318). In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:319), where n is an integer from 1 to 10. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:398), where n is 1. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:320), where n is 2. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:321), where n is 3. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:322), where n is 4. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:323), where n is 5. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ IDNO:324), where n is 6. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:325), where n is 7. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:326), where n is 8. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO: 327), where n is 9. In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:328), where n is 10.

[00146] In some cases, the peptide linker comprises the amino acid sequence CGGGS (SEQ ID NO:329). In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO: 330), where n is an integer from 1 to 10. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:331), where n is 1. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:332), where n is 2. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:333), where n is 3. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:334), where n is 4. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:335), where n is 5. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:336), where n is 6. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:337), where n is 7. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:338), where n is 8. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:339), where n is 9. In some cases, the peptide linker comprises the amino acid sequence CGGGS(GGGGS)n (SEQ ID NO:340), where n is 10.

[00147] The following are non-limiting examples of MHC Class I heavy chain comprising a Y84C substitution and an A236C substitution, based on the amino acid numbering of HLA-A*0201 (depicted in FIG. 7A), or at corresponding positions in another Class I heavy chain allele.

HLA-A

[00148] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises: a) a first polypeptide comprising: i) a peptide (e.g., a peptide of from 4 amino acids to about 25 amino acids that is bound by a TCR when the peptide is complexed with MHC polypeptides); and ii) a first MHC polypeptide, where the first polypeptide comprises a peptide linker between the peptide and the first MHC polypeptide, where the peptide linker comprises a Cys residue, and where the first MHC polypeptide is a β2M polypeptide that comprises an amino acid substitution that introduces a Cys residue; and b) a second polypeptide comprising an HLA-A MHC Class I heavy chain comprising an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET
RKVKAHSQTHRVDLGTLRG**C**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA
LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK
THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV
VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:341), where amino acid 84 is a Cys and amino acid 236 is a Cys; and c) at least one immunomodulatory polypeptide, where the first and/or the

second polypeptide comprises the at least one immunomodulatory polypeptide. In some cases, the peptide linker comprises the amino acid sequence GCGGS (SEQ ID NO:318). In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO: 319), where n is an integer from 1 to 10. In some cases, the β2M polypeptide comprises an R12C substitution. For example, the β2M polypeptide can comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence: IQRTPKIQVYS**C**HPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSFYLL YYTEFTPTEKDEYACRVNHVTLSQPKIVKWDRDM (SEQ ID NO:314), where amino acid 12 is a Cys. The at least one immunomodulatory polypeptide can be a polypeptide that exerts an activating/stimulating effect on the target T cell or a suppressing/inhibitory effect on the target T cell. For example, the at least one immunomodulatory polypeptide can be a cytokine (e.g., an IL2 polypeptide, an IL7 polypeptide, an IL12 polypeptide, an IL15 polypeptide, an IL17 polypeptide, an IL21 polypeptide, an IL27 polypeptide, an IL-23 polypeptide, a TGFβ polypeptide, and the like; and including all family members, e.g., IL17A, IL-17B, IL-17C, IL-17D, IL-17E, IL-17F, IL-17E), a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, (CD80 and CD86 are also known as B7-1 and B7-2, respectively), a CD40 polypeptide, a CD70 polypeptide, a JAG1 (CD339) polypeptide, an ICAM (CD540 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a PD-L2 polypeptide, a PD-1H (VISTA) polypeptide, an ICOS-L (CD275) polypeptide, a GITRL polypeptide, an HVEM polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, a Galectin-9 polypeptide, a CD83 polypeptide, a CD30L polypeptide, a HLA-G polypeptide, a MICA polypeptide, a MICB polypeptide, a HVEM (CD270) polypeptide, a lymphotoxin beta receptor polypeptide, a 3/TR6 polypeptide, an ILT3 polypeptide, an ILT4 polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, or a CX3CL1 polypeptide. These immunomodulatory polypeptides may be the wild type polypeptide or a variant of a wild type polypeptide. In some cases, the immunomodulatory polypeptide is an activating ("stimulatory") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide may produce an activating/stimulating effect on a T cell. Examples of activating immunomodulatory polypeptides include, e.g., CD80, CD86, 4-1BBL, OX40L, CD70, ICOS-L, CD40, ICAM (CD54), IL2, IL7, IL12, IL15, IL17, IL21, IL27, IL23, GITRL, TGFβ, and lymphotoxin beta receptor. In some cases, the immunomodulatory polypeptide is an inhibitory ("suppressing") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide s may produce a suppressing/inhibitory effect on a T cell. Examples of inhibitory immunomodulatory polypeptides include, e.g., PD-1H, PD-L1, PD-L2, TGFβ, FasL, HVEM, Galectin-9, ILT3, and ILT4. TGFβ polypeptides may produce either an activating/stimulating effect or a suppressing/inhibitory effect, depending on the context. In some cases, the at least one immunomodulatory polypeptide is a reduced

affinity variant, as described elsewhere herein. In some cases, the first or the second polypeptide comprises an Ig Fc polypeptide.

[00149] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an HLA-A Class I heavy chain polypeptide. In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the HLA-A*0101, HLA-A*0201, HLA-A*0202, HLA-A*1101, HLA-A*2301, HLA-A*2402, HLA-A*2407, HLA-A*3303, or HLA-A*3401 amino acid sequence depicted in FIG. 7A, where the HLA-A heavy chain polypeptide comprises Y84C and A236C substitutions.

HLA-A*0101 (Y84C; A236C)

[00150] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*0101 (Y84C; A236C) amino acid sequence:

[00151] GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQKMEPRAPWIEQE GPEYWDQETRNMKAHSQTDRANLGTLRG**C**YNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDA YDGKDYIALNEDLRSWTAADMAAQITKRKWEAVHAAEQRRVYLEGRCVDGLRRYLENGKET LQRTDPPKTHMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTF QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:343), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-A*0201 (Y84C; A236C)

[00152] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*0201 (Y84C; A236C) amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRG**C**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:341), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-A*0202 (Y84C; A236C)

[00153] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*0202 (Y84C; A236C) amino acid sequence: GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDGET RKVKAHSQTHRVDLGTLRG**C**YNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDGKDYIA LKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQRTDAPK THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:341), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-A*1101 (Y84C; A236C)

[00154] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*1101 (Y84C; A236C) amino acid sequence: GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDQE TRNVKAQSQTDRVDLGTLRG**C**YNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDGKDYIA LNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAYLEGRCVEWLRRYLENGKETLQRTDPPK THMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVV VPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:344), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-A*2301 (Y84C; A236C)

[00155] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*2301 (Y84C; A236C) amino acid sequence: GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDEET GKVKAHSQTDRENLRIALR**C**YNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDGKDYIAL KEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVDGLRRYLENGKETLQRTDPPKTH MTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVVPS GEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:345), where amino acid 84 is a Cys and amino acid 236 is a Cys.

*HLA-A*2402 (Y84C; A236C)*

[00156] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*2402 (Y84C; A236C) amino acid sequence: GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDEET GKVKAHSQTDRENLRIALR**C**YNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDGKDYIAL KEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQRTDPPKT HMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVV PSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:346), where amino acid 84 is a Cys and amino acid 236 is a Cys.

*HLA-A*2407 (Y84C; A236C)*

[00157] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*2407 (Y84C; A236C) amino acid sequence: GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDEET GKVKAQSQTDRENLRIALR**C**YNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDGKDYIAL KEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQRTDPPKT HMTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVV PSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:347), where amino acid 84 is a Cys and amino acid 236 is a Cys.

*HLA-A*3303 (Y84C; A236C)*

[00158] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*3303 (Y84C; A236C) amino acid sequence:

[00159] GSHSMRYFTTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE GPEYWDRNTRNVKAHSQIDRVDLGTLRG**C**YNQSEAGSHTIQMMYGCDVGSDGRFLRGYQQD AYDGKDYIALNEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVEWLRRYLENGKE TLQRTDPPKTHMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGT FQKWASVVVPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:348), where amino acid 84 is a Cys and amino acid 236 is a Cys.

*HLA-A*3401 (Y84C; A236C)*

[00160] In some cases, the HLA-A heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-A*3401 (Y84C; A236C) amino acid sequence:
GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYWDRN
TRKVKAQSQTDRVDLGTLRG**C**YNQSEDGSHTIQRMYGCDVGPDGRFLRGYQQDAYDGKDYIA
LNEDLRSWTAADMAAQITQRKWETAHEAEQWRAYLEGTCVEWLRRYLENGKETLQRTDAPK
THMTHHAVSDHEATLRCWALSFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWASVV
VPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:349), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B

[00161] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises: a) a first polypeptide comprising: i) a peptide (e.g., a peptide of from 4 amino acids to about 25 amino acids that is bound by a TCR when the peptide is complexed with MHC polypeptides); and ii) a first MHC polypeptide, where the first polypeptide comprises a peptide linker between the peptide and the first MHC polypeptide, where the peptide linker comprises a Cys residue, and where the first MHC polypeptide is a β2M polypeptide that comprises an amino acid substitution that introduces a Cys residue; and b) a second polypeptide comprising an HLA-B MHC Class I heavy chain comprising an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:
GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYWDRNT
QIYKAQAQTDRESLRNLRG**C**YNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDGKDYIAL
NEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLERADPPKTH
VTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQKWAAVVVPS
GEEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:350), where amino acid 84 is a Cys and amino acid 236 is a Cys; and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the at least one immunomodulatory polypeptide. In some cases, the peptide linker comprises the amino acid sequence GCGGS (SEQ ID NO:318). In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:342), where n is an integer from 1 to 10. In some cases, the β2M polypeptide comprises an R12C substitution. For example, the β2M polypeptide can comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:
IQRTPKIQVYS**C**HPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSFYLL

YYTEFTPTEKDEYACRVNHVTLSQPKIVKWDRDM (SEQ ID NO:314), where amino acid 12 is a Cys. The at least one immunomodulatory polypeptide can be a polypeptide that exerts an activating/stimulating effect on the target T cell or a suppressing/inhibitory effect on the target T cell. For example, the at least one immunomodulatory polypeptide can be a cytokine (e.g., an IL2 polypeptide, an IL7 polypeptide, an IL12 polypeptide, an IL15 polypeptide, an IL17 polypeptide, an IL21 polypeptide, an IL27 polypeptide, an IL-23 polypeptide, a TGFβ polypeptide, and the like; and including all family members, e.g., IL17A, IL-17B, IL-17C, IL-17D, IL-17E, IL-17F, IL-17E), a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, (CD80 and CD86 are also known as B7-1 and B7-2, respectively), a CD40 polypeptide, a CD70 polypeptide, a JAG1 (CD339) polypeptide, an ICAM (CD540 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a PD-L2 polypeptide, a PD-1H (VISTA) polypeptide, an ICOS-L (CD275) polypeptide, a GITRL polypeptide, an HVEM polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, a Galectin-9 polypeptide, a CD83 polypeptide, a CD30L polypeptide, a HLA-G polypeptide, a MICA polypeptide, a MICB polypeptide, a HVEM (CD270) polypeptide, a lymphotoxin beta receptor polypeptide, a 3/TR6 polypeptide, an ILT3 polypeptide, an ILT4 polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, or a CX3CL1 polypeptide. These immunomodulatory polypeptides may be the wild type polypeptide or a variant of a wild type polypeptide. In some cases, the immunomodulatory polypeptide is an activating ("stimulatory") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide may produce an activating/stimulating effect on a T cell. Examples of activating immunomodulatory polypeptides include, e.g., CD80, CD86, 4-1BBL, OX40L, CD70, ICOS-L, CD40, ICAM (CD54), IL2, IL7, IL12, IL15, IL17, IL21, IL27, IL23, GITRL, TGFβ, and lymphotoxin beta receptor. In some cases, the immunomodulatory polypeptide is an inhibitory ("suppressing") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide s may produce a suppressing/inhibitory effect on a T cell. Examples of inhibitory immunomodulatory polypeptides include, e.g., PD-1H, PD-L1, PD-L2, TGFβ, FasL, HVEM, Galectin-9, ILT3, and ILT4. TGFβ polypeptides may produce either an activating/stimulating effect or a suppressing/inhibitory effect, depending on the context. In some cases, the at least one immunomodulatory polypeptide is a reduced affinity variant, as described elsewhere herein. In some cases, the first or the second polypeptide comprises an Ig Fc polypeptide.

[00162] In some cases, a multiple disulfide-linked TMMP of the present disclosure comprises an HLA-B Class I heavy chain polypeptide. In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the HLA-B*0702, HLA-B*0801, HLA-B*1502, HLA-B*3802, HLA-B*4001,

HLA-B*4601, or HLA-B*5301 amino acid sequence depicted in FIG. 8A, where the HLA-B heavy chain polypeptide comprises Y84C and A236C substitutions.

HLA-B*0702 (Y84C; A236C)

[00163] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*0702 (Y84C; A236C) amino acid sequence:

[00164] GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE GPEYWDRNTQIYKAQAQTDRESLRNLRG**C**YNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYA YDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKL ERADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQK WAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:350), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*0801 (Y84C; A236C)

[00165] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*0801 (Y84C; A236C) amino acid sequence:

[00166] GSHSMRYFDTAMSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE GPEYWDRNTQIFKTNTQTDRESLRNLRG**C**YNQSEAGSHTLQSMYGCDVGPDGRLLRGHNQYA YDGKDYIALNEDLRSWTAADTAAQITQRKWEAARVAEQDRAYLEGTCVEWLRRYLENGKDTL ERADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQK WAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:351), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*1502 (Y84C; A236C)

[00167] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*1502 (Y84C; A236C) amino acid sequence:

[00168] GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRMAPRAPWIEQ EGPEYWDRNTQISKTNTQTYRESLRNLRG**C**YNQSEAGSHIIQRMYGCDVGPDGRLLRGYDQSA YDGKDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQLRAYLEGLCVEWLRRYLENGKETL QRADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQ

KWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:352), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*3802 (Y84C; A236C)

[00169] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*3802 (Y84C; A236C) amino acid sequence:

[00170] GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE GPEYWDRNTQICKTNTQTYRENLRTALR**C**YNQSEAGSHTLQRMYGCDVGPDGRLLRGHNQFA YDGKDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRTYLEGTCVEWLRRYLENGKETL QRADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQ KWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:353), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*4001 (Y84C; A2346C)

[00171] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*4001 (Y84C; A236C) amino acid sequence:

[00172] GSHSMRYFHTAMSRPGRGEPRFITVGYVDDTLFVRFDSDATSPRKEPRAPWIEQE GPEYWDRETQISKTNTQTYRESLRNLRG**C**YNQSEAGSHTLQRMYGCDVGPDGRLLRGHNQYA YDGKDYIALNEDLRSWTAADTAAQISQRKLEAARVAEQLRAYLEGECVEWLRRYLENGKDKL ERADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQK WAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:354) where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*4601 (Y84C; A236C)

[00173] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*4601 (Y84C; A236C) amino acid sequence:

[00174] GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRMAPRAPWIEQ EGPEYWDRETQKYKRQAQTDRVSLRNLRG**C**YNQSEAGSHTLQRMYGCDVGPDGRLLRGHDQ SAYDGKDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQWRAYLEGLCVEWLRRYLENGKE TLQRADPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTF

QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:355) where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-B*5301 (Y84C; A236C)

[00175] In some cases, the HLA-B heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-B*5301 (Y84C; A236C) amino acid sequence:

[00176] GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRTEPRAPWIEQE GPEYWDRNTQIFKTNTQTYRENLRIALR**C**YNQSEAGSHIIQRMYGCDLGPDGRLLRGHDQSAY DGKDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRAYLEGLCVEWLRRYLENGKETLQ RADPPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDRTFQK WAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:356) where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C

[00177] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises: a) a first polypeptide comprising: i) a peptide (e.g., a peptide of from 4 amino acids to about 25 amino acids that is bound by a TCR when the peptide is complexed with MHC polypeptides); and ii) a first MHC polypeptide, where the first polypeptide comprises a peptide linker between the peptide and the first MHC polypeptide, where the peptide linker comprises a Cys residue, and where the first MHC polypeptide is a β2M polypeptide that comprises an amino acid substitution that introduces a Cys residue; and b) a second polypeptide comprising an HLA-C MHC Class I heavy chain comprising an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:

CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYWDRE TQNYKRQAQADRVSLRNLRG**C**YNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQSAYDGKDYI ALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKETLQRAEPPKT HVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRP**C**GDGTFQKWAAVVV PSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:357), where amino acid 84 is a Cys and amino acid 236 is a Cys; and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the at least one immunomodulatory polypeptide. In some cases, the peptide linker comprises the amino acid sequence GCGGS (SEQ ID NO:318). In some cases, the peptide linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:342), where n is an integer from 1 to 10. In some cases, the β2M polypeptide comprises an R12C substitution. For example, the β2M polypeptide can comprises an amino acid sequence having at least 90%, at least 95%, at least 98%,

at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence: IQRTPKIQVYSCHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSFSKDWSFYLL YYTEFTPTEKDEYACRVNHVTLSQPKIVKWDRDM (SEQ ID NO:314), where amino acid 12 is a Cys. The at least one immunomodulatory polypeptide can be a polypeptide that exerts an activating/stimulating effect on the target T cell or a suppressing/inhibitory effect on the target T cell. For example, the at least one immunomodulatory polypeptide can be a cytokine (e.g., an IL2 polypeptide, an IL7 polypeptide, an IL12 polypeptide, an IL15 polypeptide, an IL17 polypeptide, an IL21 polypeptide, an IL27 polypeptide, an IL-23 polypeptide, a TGFβ polypeptide, and the like; and including all family members, e.g., IL17A, IL-17B, IL-17C, IL-17D, IL-17E, IL-17F, IL-17E), a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, (CD80 and CD86 are also known as B7-1 and B7-2, respectively), a CD40 polypeptide, a CD70 polypeptide, a JAG1 (CD339) polypeptide, an ICAM (CD540 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a PD-L2 polypeptide, a PD-1H (VISTA) polypeptide, an ICOS-L (CD275) polypeptide, a GITRL polypeptide, an HVEM polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, a Galectin-9 polypeptide, a CD83 polypeptide, a CD30L polypeptide, a HLA-G polypeptide, a MICA polypeptide, a MICB polypeptide, a HVEM (CD270) polypeptide, a lymphotoxin beta receptor polypeptide, a 3/TR6 polypeptide, an ILT3 polypeptide, an ILT4 polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, or a CX3CL1 polypeptide. These immunomodulatory polypeptides may be the wild type polypeptide or a variant of a wild type polypeptide. In some cases, the immunomodulatory polypeptide is an activating ("stimulatory") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide may produce an activating/stimulating effect on a T cell. Examples of activating immunomodulatory polypeptides include, e.g., CD80, CD86, 4-1BBL, OX40L, CD70, ICOS-L, CD40, ICAM (CD54), IL2, IL7, IL12, IL15, IL17, IL21, IL27, IL23, GITRL, TGFβ, and lymphotoxin beta receptor. In some cases, the immunomodulatory polypeptide is an inhibitory ("suppressing") immunomodulatory polypeptide; e.g., the immunomodulatory polypeptide s may produce a suppressing/inhibitory effect on a T cell. Examples of inhibitory immunomodulatory polypeptides include, e.g., PD-1H, PD-L1, PD-L2, TGFβ, FasL, HVEM, Galectin-9, ILT3, and ILT4. TGFβ polypeptides may produce either an activating/stimulating effect or a suppressing/inhibitory effect, depending on the context. In some cases, the at least one immunomodulatory polypeptide is a reduced affinity variant, as described elsewhere herein. In some cases, the first or the second polypeptide comprises an Ig Fc polypeptide.

[00178] In some cases, a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an HLA-C Class I heavy chain polypeptide. In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a

double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the HLA-C*0102, HLA-C*0303, HLA-C*0304, HLA-C*0401, HLA-C*0602, HLA-C*0701, HLA-C*0702, HLA-C*0801, or HLA-C*1502 amino acid sequence depicted in FIG. 9A, where the HLA-C heavy chain polypeptide comprises Y84C and A236C substitutions.

HLA-C*01:02 (Y84C; A236C)

[00179] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*01:02 (Y84C; A236C) amino acid sequence:

[00180] CSHSMKYFFTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQE GPEYWDRETQKYKRQAQTDRVSLRNLRG**C**YNQSEAGSHTLQWMCGCDLGPDGRLLRGYDQY AYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGTCVEWLRRYLENGKET LQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQWDGEDQTQDTELVETRP**C**GDGTF QKWAAVMVPSGEEQRYTCHVQHEGLPEPLTLRWEP (SEQ ID NO:358), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0303 (Y84C; A236C)

[00181] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*03:03 (Y84C; A236C) amino acid sequence:

[00182] GSHSMRYFYTAVSRPGRGEPHFIAVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQKYKRQAQTDRVSLRNLRG**C**YNQSEARSHIIQRMYGCDVGPDGRLLRGYDQY AYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQLRAYLEGLCVEWLRRYLKNGKET LQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQWDGEDQTQDTELVETRP**C**GDGTF QKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWEP (SEQ ID NO:359), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0304 (Y84C; A236C)

[00183] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*03:04 (Y84C; A236C) amino acid sequence:

[00184] GSHSMRYFYTAVSRPGRGEPHFIAVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQKYKRQAQTDRVSLRNLRG**C**YNQSEAGSHIIQRMYGCDVGPDGRLLRGYDQY

AYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQLRAYLEGLCVEWLRRYLKNGKET LQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQWDGEDQTQDTELVETRPCGDGTF QKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWEP (SEQ ID NO:360), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0401 (Y84C; A236C)

[00185] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*04:01 (Y84C; A236C) amino acid sequence:

[00186] GSHSMRYFSTSVSWPGRGEPRFIAVGYVDDTQFVRFDSDAASPRGEPREPWVEQ EGPEYWDRETQKYKRQAQADRVNLRKLRGCYNQSEDGSHTLQRMFGCDLGPDGRLLRGYNQ FAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGTCVEWLRRYLENGKE TLQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQWDGEDQTQDTELVETRPCGDGT FQKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWKP (SEQ ID NO:361), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0602 (Y84C; A236C)

[00187] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*06:02 (Y84C; A236C) amino acid sequence:

[00188] CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQKYKRQAQADRVNLRKLRGCYNQSEDGSHTLQWMYGCDLGPDGRLLRGYD QSAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQWRAYLEGTCVEWLRRYLENG KETLQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPCGD GTFQKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWEP (SEQ ID NO:362), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0701 (Y84C; A236C)

[00189] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*07:01 (Y84C; A236C) amino acid sequence:

[00190] CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQNYKRQAQADRVSLRNLRGCYNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQ SAYDGKDYIALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKE

TLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPCGDGT FQKWAAVVVPSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:357), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0702 (Y84C; A236C)

[00191] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*07:02 (Y84C; A236C) amino acid sequence:

[00192] CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQKYKRQAQADRVSLRNLRGCYNQSEDGSHTLQRMSGCDLGPDGRLLRGYDQS AYDGKDYIALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKET LQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPCGDGTF QKWAAVVVPSGQEQRYTCHMQHEGLQEPLTLSWEP (SEQ ID NO:404), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*0801 (Y84C; A236C)

[00193] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*08:01 (Y84C; A236C) amino acid sequence:

[00194] CSHSMRYFYTAVSRPGRGEPRFIAVGYVDDTQFVQFDSDAASPRGEPRAPWVEQ EGPEYWDRETQKYKRQAQTDRVSLRNLRGCYNQSEAGSHTLQRMYGCDLGPDGRLLRGYNQ FAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAARTAEQLRAYLEGTCVEWLRRYLENGKK TLQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPCGDGT FQKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWGP (SEQ ID NO:363), where amino acid 84 is a Cys and amino acid 236 is a Cys.

HLA-C*1502 (Y84C; A236C)

[00195] In some cases, the HLA-C heavy chain polypeptide present in a multiple disulfide-linked TMMP of the present disclosure (e.g., a double disulfide-linked TMMP) comprises an amino acid sequence having at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following HLA-C*15:02 (Y84C; A236C) amino acid sequence:

[00196] CSHSMRYFYTAVSRPGRGEPHFIAVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ EGPEYWDRETQNYKRQAQTDRVNLRKLRGCYNQSEAGSHIIQRMYGCDLGPDGRLLRGHDQL AYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQLRAYLEGTCVEWLRRYLENGKET LQRAEHPKTHVTHHPVSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPCGDGTF

QKWAAVVVPSGEEQRYTCHVQHEGLPEPLTLRWEP (SEQ ID NO:364), where amino acid 84 is a Cys and amino acid 236 is a Cys.

Scaffold polypeptides

[00197] A TMMP can comprise an Fc polypeptide, or can comprise another suitable scaffold polypeptide.

[00198] Suitable scaffold polypeptides include antibody-based scaffold polypeptides and non-antibody-based scaffolds. Non-antibody-based scaffolds include, e.g., albumin, an XTEN (extended recombinant) polypeptide, transferrin, an Fc receptor polypeptide, an elastin-like polypeptide (see, e.g., Hassouneh et al. (2012) *Methods Enzymol.* 502:215; e.g., a polypeptide comprising a pentapeptide repeat unit of (Val-Pro-Gly-X-Gly; SEQ ID NO:59), where X is any amino acid other than proline), an albumin-binding polypeptide, a silk-like polypeptide (see, e.g., Valluzzi et al. (2002) *Philos Trans R Soc Lond B Biol Sci.* 357:165), a silk-elastin-like polypeptide (SELP; see, e.g., Megeed et al. (2002) *Adv Drug Deliv Rev.* 54:1075), and the like. Suitable XTEN polypeptides include, e.g., those disclosed in WO 2009/023270, WO 2010/091122, WO 2007/103515, US 2010/0189682, and US 2009/0092582; see also Schellenberger et al. (2009) *Nat Biotechnol.* 27:1186). Suitable albumin polypeptides include, e.g., human serum albumin.

[00199] Suitable scaffold polypeptides will in some cases be a half-life extending polypeptides. Thus, in some cases, a suitable scaffold polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the TMMP, compared to a control TMMP lacking the scaffold polypeptide. For example, in some cases, a scaffold polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the TMMP, compared to a control TMMP lacking the scaffold polypeptide, by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 50%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold. As an example, in some cases, an Fc polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the TMMP, compared to a control TMMP lacking the Fc polypeptide, by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 50%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold.

Fc polypeptides

[00200] In some cases, the first and/or the second polypeptide chain of a TMMP of the present disclosure comprises an Fc polypeptide. The Fc polypeptide of a TMMP of the present disclosure can be a human IgG1 Fc, a human IgG2 Fc, a human IgG3 Fc, a human IgG4 Fc, etc. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to an amino acid sequence of an Fc region depicted in FIG.

3A-3G. In some cases, the Fc region comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in FIG. 3A. In some cases, the Fc region comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in FIG. 3A; and comprises a substitution of N77; e.g., the Fc polypeptide comprises an N77A substitution. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG2 Fc polypeptide depicted in FIG. 3A; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 99-325 of the human IgG2 Fc polypeptide depicted in FIG. 3A. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG3 Fc polypeptide depicted in FIG. 3A; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 19-246 of the human IgG3 Fc polypeptide depicted in FIG. 3A. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgM Fc polypeptide depicted in FIG. 3B; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 1-276 to the human IgM Fc polypeptide depicted in FIG. 3B. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgA Fc polypeptide depicted in FIG. 3C; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 1-234 to the human IgA Fc polypeptide depicted in FIG. 3C.

[00201] In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG4 Fc polypeptide depicted in FIG. 3C. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 100 to 327 of the human IgG4 Fc polypeptide depicted in FIG. 3C.

[00202] In some cases, the IgG4 Fc polypeptide comprises the following amino acid sequence: PPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA KTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:365).

[00203] In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc). In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for a substitution of N297 (N77 of the amino acid sequence depicted in FIG. 3A) with an amino acid other than asparagine. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3C (human IgG1 Fc comprising an N297A substitution, which is N77 of the amino acid sequence depicted in FIG. 3A). In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for a substitution of L234 (L14 of the amino acid sequence depicted in FIG. 3A) with an amino acid other than leucine. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for a substitution of L235 (L15 of the amino acid sequence depicted in FIG. 3A) with an amino acid other than leucine.

[00204] In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3E. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3F. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 5G (human IgG1 Fc comprising an L234A substitution and an L235A substitution, corresponding to positions 14 and 15 of the amino acid sequence depicted in FIG. 3G). In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for a substitution of P331 (P111 of the amino acid sequence depicted in FIG. 3A) with an amino acid other than proline; in some cases, the substitution is a P331S substitution. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for substitutions at L234 and L235 (L14 and L15 of the amino acid sequence depicted in FIG. 3A) with amino acids other than leucine. In some cases, the Fc

polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3A (human IgG1 Fc), except for substitutions at L234 and L235 (L14 and L15 of the amino acid sequence depicted in FIG. 3A) with amino acids other than leucine, and a substitution of P331 (P111 of the amino acid sequence depicted in FIG. 3A) with an amino acid other than proline. In some cases, the Fc polypeptide present in a TMMP comprises the amino acid sequence depicted in FIG. 3E (human IgG1 Fc comprising L234F, L235E, and P331S substitutions (corresponding to amino acid positions 14, 15, and 111 of the amino acid sequence depicted in FIG. 3E). In some cases, the Fc polypeptide present in a TMMP is an IgG1 Fc polypeptide that comprises L234A and L235A substitutions (substitutions of L14 and L15 of the amino acid sequence depicted in FIG. 3A with Ala), as depicted in FIG. 3G.

Linkers

[00205] A TMMP of the present disclosure can include one or more linkers, where the one or more linkers are between one or more of: i) an MHC Class I polypeptide and an Ig Fc polypeptide, where such a linker is referred to herein as "L1"; ii) an immunomodulatory polypeptide and an MHC Class I polypeptide, where such a linker is referred to herein as "L2"; iii) a first immunomodulatory polypeptide and a second immunomodulatory polypeptide, where such a linker is referred to herein as "L3"; iv) a peptide antigen ("epitope") and an MHC Class I polypeptide; v) an MHC Class I polypeptide and a dimerization polypeptide (e.g., a first or a second member of a dimerizing pair); and vi) a dimerization polypeptide (e.g., a first or a second member of a dimerizing pair) and an IgFc polypeptide.

[00206] Suitable linkers (also referred to as "spacers") can be readily selected and can be of any of a number of suitable lengths, such as from 1 amino acid to 25 amino acids, from 3 amino acids to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids. A suitable linker can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids in length. In some cases, a linker has a length of from 25 amino acids to 50 amino acids, e.g., from 25 to 30, from 30 to 35, from 35 to 40, from 40 to 45, or from 45 to 50 amino acids in length.

[00207] Exemplary linkers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $(GSGGS)_n$ (SEQ ID NO:366) and $(GGGS)_n$ (SEQ ID NO:367), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers can be used; both Gly and Ser are relatively unstructured, and therefore can serve as a neutral tether between components. Glycine polymers can be used; glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary linkers can comprise amino acid sequences including, but not limited to, GGSG (SEQ ID NO:368), GGSGG (SEQ ID NO:369), GSGSG (SEQ ID NO:370), GSGGG (SEQ ID NO:371), GGGSG (SEQ ID NO:372),

GSSSG (SEQ ID NO:373), and the like. Exemplary linkers can include, e.g., Gly(Ser$_4$)n (SEQ ID NO:374), where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some cases, a linker comprises the amino acid sequence (GSSSS)n (SEQ ID NO:375), where n is 4. In some cases, a linker comprises the amino acid sequence (GSSSS)n (SEQ ID NO:376), where n is 5. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:377), where n is 1. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:378), where n is 2. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:379), where n is 3. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:380), where n is 4. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:381), where n is 5. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:382), where n is 6. In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:383), where n is 7, In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:384), where n is 8, In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:385), where n is 9, In some cases, a linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO:386), where n is 10. In some cases, a linker comprises the amino acid sequence AAAGG (SEQ ID NO:387).

[00208] In some cases, a linker polypeptide, present in a first polypeptide of a TMMP of the present disclosure, includes a cysteine residue that can form a disulfide bond with a cysteine residue present in a second polypeptide of a TMMP of the present disclosure. In some cases, for example, a suitable linker comprises the amino acid sequence G**C**GGSGGGGSGGGGS (SEQ ID NO:317). As another example, a suitable linker can comprise the amino acid sequence GCGGS(G4S)n (SEQ ID NO:315), where n is 1, 2, 3, 4, 5, 6, 7, 8, or 9. For example, in some cases, the linker comprises the amino acid sequence GCGGSGGGGSGGGGSGGGGS (SEQ ID NO:316). As another example, the linker comprises the amino acid sequence GCGGSGGGGSGGGGS (SEQ ID NO:317).

Epitopes

[00209] A TMMP of the present disclosure comprises any of a variety of peptide epitopes. A TMMP comprises a peptide that, when in an MHC/peptide complex (e.g., an HLA/peptide complex), presents an epitope to a T cell. A peptide, present in a TMMP of the present disclosure, that, when in an MHC/peptide complex (e.g., an HLA/peptide complex), presents an epitope to a T cell, is referred to herein as a "peptide epitope" or, simply, an "epitope."

[00210] An epitope present in a TMMP of the present disclosure can have a length of from about 4 amino acids to about 25 amino acids, e.g., the epitope can have a length of from 4 amino acids (aa) to 10 aa, from 10 aa to 15 aa, from 15 aa to 20 aa, or from 20 aa to 25 aa. For example, an epitope present in a TMMP of the present disclosure can have a length of 4 amino acids (aa), 5 aa, 6 aa, 7, aa, 8 aa, 9 aa, 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, 20 aa, 21 aa, 22 aa, 23 aa, 24 aa, or 25

aa. In some cases, an epitope present in a TMMP of the present disclosure has a length of from 5 amino acids to 10 amino acids, e.g., 5 aa, 6 aa, 7 aa, 8 aa, 9 aa, or 10 aa.

[00211] An epitope present in a TMMP of the present disclosure is a peptide specifically bound by a T-cell, i.e., the epitope is specifically bound by an epitope-specific T cell. An epitope-specific T cell binds an epitope having a reference amino acid sequence, but does not substantially bind an epitope that differs from the reference amino acid sequence. For example, an epitope-specific T cell binds an epitope having a reference amino acid sequence, and binds an epitope that differs from the reference amino acid sequence, if at all, with an affinity that is less than 10^{-6} M, less than 10^{-5} M, or less than 10^{-4} M. An epitope-specific T cell can bind an epitope for which it is specific with an affinity of at least 10^{-7} M, at least 10^{-8} M, at least 10^{-9} M, or at least 10^{-10} M.

[00212] Suitable epitopes include, but are not limited to, epitopes present in a cancer-associated antigen. Cancer-associated antigens are known in the art; see, e.g., Cheever et al. (2009) *Clin. Cancer Res.* 15:5323. Cancer-associated antigens include, but are not limited to, α-folate receptor; carbonic anhydrase IX (CAIX); CD19; CD20; CD22; CD30; CD33; CD44v7/8; carcinoembryonic antigen (CEA); epithelial glycoprotein-2 (EGP-2); epithelial glycoprotein-40 (EGP-40); folate binding protein (FBP); fetal acetylcholine receptor; ganglioside antigen GD2; Her2/neu; IL-13R-a2; kappa light chain; LeY; L1 cell adhesion molecule; melanoma-associated antigen (MAGE); MAGE-A1; mesothelin; MUC1; NKG2D ligands; oncofetal antigen (h5T4); prostate stem cell antigen (PSCA); prostate-specific membrane antigen (PSMA); tumor-associate glycoprotein-72 (TAG-72); vascular endothelial growth factor receptor-2 (VEGF-R2). See, e.g., Vigneron et al. (2013) *Cancer Immunity* 13:15; and Vigneron (2015) *BioMed Res. Int'l* Article ID 948501; and epidermal growth factor receptor (EGFR) vIII polypeptide (see, e.g., Wong et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:2965; and Miao et al. (2014) *PLoSOne* 9:e94281).

[00213] In some cases, a suitable peptide epitope is a peptide fragment of from about 4 amino acids to about 20 amino acids (e.g., 4 amino acids (aa), 5 aa, 6 aa, 7 aa, 8 aa, 9 aa, 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, or 20 aa) in length of a MUC1 polypeptide, an LMP2 polypeptide, an epidermal growth factor receptor (EGFR) vIII polypeptide, a HER-2/neu polypeptide, a melanoma antigen family A, 3 (MAGE A3) polypeptide, a p53 polypeptide, a mutant p53 polypeptide, an NY-ESO-1 polypeptide, a folate hydrolase (prostate-specific membrane antigen; PSMA) polypeptide, a carcinoembryonic antigen (CEA) polypeptide, a melanoma antigen recognized by T-cells (melanA/MART1) polypeptide, a Ras polypeptide, a gp100 polypeptide, a proteinase3 (PR1) polypeptide, a bcr-abl polypeptide, a tyrosinase polypeptide, a survivin polypeptide, a prostate specific antigen (PSA) polypeptide, an hTERT polypeptide, a sarcoma translocation breakpoints polypeptide, a synovial sarcoma X (SSX) breakpoint polypeptide, an EphA2 polypeptide, an acid phosphatase, prostate (PAP) polypeptide, a melanoma inhibitor of apoptosis (ML-IAP) polypeptide, an epithelial cell adhesion

molecule (EpCAM) polypeptide, an ERG (TMPRSS2 ETS fusion) polypeptide, a NA17 polypeptide, a paired-box-3 (PAX3) polypeptide, an anaplastic lymphoma kinase (ALK) polypeptide, an androgen receptor polypeptide, a cyclin B1 polypeptide, an N-myc proto-oncogene (MYCN) polypeptide, a Ras homolog gene family member C (RhoC) polypeptide, a tyrosinase-related protein-2 (TRP-2) polypeptide, a mesothelin polypeptide, a prostate stem cell antigen (PSCA) polypeptide, a melanoma associated antigen-1 (MAGE A1) polypeptide, a cytochrome P450 1B1 (CYP1B1) polypeptide, a placenta-specific protein 1 (PLAC1) polypeptide, a BORIS polypeptide (also known as CCCTC-binding factor or CTCF), an ETV6-AML polypeptide, a breast cancer antigen NY-BR-1 polypeptide (also referred to as ankyrin repeat domain-containing protein 30A), a regulator of G-protein signaling (RGS5) polypeptide, a squamous cell carcinoma antigen recognized by T-cells (SART3) polypeptide, a carbonic anhydrase IX polypeptide, a paired box-5 (PAX5) polypeptide, an OY-TES1 (testis antigen; also known as acrosin binding protein) polypeptide, a sperm protein 17 polypeptide, a lymphocyte cell-specific protein-tyrosine kinase (LCK) polypeptide, a high molecular weight melanoma associated antigen (HMW-MAA), an A-kinase anchoring protein-4 (AKAP-4), a synovial sarcoma X breakpoint 2 (SSX2) polypeptide, an X antigen family member 1 (XAGE1) polypeptide, a B7 homolog 3 (B7H3; also known as CD276) polypeptide, a legumain polypeptide (LGMN1; also known as asparaginyl endopeptidase), a tyrosine kinase with Ig and EGF homology domains-2 (Tie-2; also known as angiopoietin-1 receptor) polypeptide, a P antigen family member 4 (PAGE4) polypeptide, a vascular endothelial growth factor receptor 2 (VEGF2) polypeptide, a MAD-CT-1 polypeptide, a fibroblast activation protein (FAP) polypeptide, a platelet derived growth factor receptor beta (PDGFβ) polypeptide, a MAD-CT-2 polypeptide, or a Fos-related antigen-1 (FOSL) polypeptide. In some cases, a human papilloma virus (HPV) antigen is specifically excluded. In some cases, an alpha-feto protein (AFP) antigen is specifically excluded. In some cases, a Wilms tumor-1 (WT1) antigen is specifically excluded.

[00214] Amino acid sequences of cancer-associated antigens are known in the art; see, e.g., MUC1 (GenBank CAA56734); LMP2 (GenBank CAA47024); EGFRvIII (GenBank NP_001333870); HER-2/neu (GenBank AAI67147); MAGE-A3 (GenBank AAH11744); p53 (GenBank BAC16799); NY-ESO-1 (GenBank CAA05908); PSMA (GenBank AAH25672); CEA (GenBank AAA51967); melan/MART1 (GenBank NP_005502); Ras (GenBank NP_001123914); gp100 (GenBank AAC60634); bcr-abl (GenBank AAB60388); tyrosinase (GenBank AAB60319); survivin (GenBank AAC51660); PSA (GenBank CAD54617); hTERT (GenBank BAC11010); SSX (GenBank NP_001265620); Eph2A (GenBank NP_004422); PAP (GenBank AAH16344); ML-IAP (GenBank AAH14475); EpCAM (GenBank NP_002345); ERG (TMPRSS2 ETS fusion) (GenBank ACA81385); PAX3 (GenBank AAI01301); ALK (GenBank NP_004295); androgen receptor (GenBank NP_000035); cyclin B1 (GenBank CAO99273); MYCN (GenBank NP_001280157); RhoC (GenBank AAH52808); TRP-2 (GenBank AAC60627); mesothelin (GenBank AAH09272); PSCA (GenBank AAH65183); MAGE A1

(GenBank NP_004979); CYP1B1 (GenBank AAM50512); PLAC1 (GenBank AAG22596); BORIS (GenBank NP_001255969); ETV6 (GenBank NP_001978); NY-BR1 (GenBank NP_443723); SART3 (GenBank NP_055521); carbonic anhydrase IX (GenBank EAW58359); PAX5 (GenBank NP_057953); OY-TES1 (GenBank NP_115878); sperm protein 17 (GenBank AAK20878); LCK (GenBank NP_001036236); HMW-MAA (GenBank NP_001888); AKAP-4 (GenBank NP_003877); SSX2 (GenBank CAA60111); XAGE1 (GenBank NP_001091073; XP_001125834; XP_001125856; and XP_001125872); B7H3 (GenBank NP_001019907; XP_947368; XP_950958; XP_950960; XP_950962; XP_950963; XP_950965; and XP_950967); LGMN1 (GenBank NP_001008530); TIE-2 (GenBank NP_000450); PAGE4 (GenBank NP_001305806); VEGFR2 (GenBank NP_002244); MAD-CT-1 (GenBank NP_005893 NP_056215); FAP (GenBank NP_004451); PDGFβ (GenBank NP_002600); MAD-CT-2 (GenBank NP_001138574); and FOSL (GenBank NP_005429). These polypeptides are also discussed in, e.g., Cheever et al. (2009) *Clin. Cancer Res.* 15:5323, and references cited therein; Wagner et al. (2003) *J. Cell. Sci.* 116:1653; Matsui et al. (1990) *Oncogene* 5:249; Zhang et al. (1996) *Nature* 383:168.

[00215] Suitable epitopes include, but are not limited to, epitopes present in an infectious disease agent, e.g., an epitope presented by a virus-encoded polypeptide. Examples of viral infectious disease agents include, e.g., Adenoviruses, Adeno-associated virus, Alphaviruses (Togaviruses), Eastern equine encephalitis virus, Eastern equine encephalomyelitis virus, Venezuelan equine encephalomyelitis vaccine strain TC-83, Western equine encephalomyelitis virus, Arenaviruses, Lymphocytic choriomeningitis virus (non-neurotropic strains), Tacaribe virus complex, Bunyaviruses, Bunyamwera virus, Rift Valley fever virus vaccine strain MP-12, Chikungunya virus, Calciviruses, Coronaviruses, Cowpox virus, Flaviviruses (Togaviruses)-Group B Arboviruses, Dengue virus serotypes 1, 2, 3, and 4, Yellow fever virus vaccine strain 17D, Hepatitis A, B, C, D, and E viruses, the Cytomegalovirus, Epstein Barr virus, Eastern Equine encephalitis virus, Herpes simplex types 1 and 2, Herpes zoster, Human herpesvirus types 6 and 7, hepatitis C virus (HVC), hepatitis B virus (HBV), Influenza viruses types A, B, and C, Papovaviruses, Newcastle disease virus, Measles virus, Mumps virus, Parainfluenza viruses types 1, 2, 3, and 4, polyomaviruses (JC virus, BK virus), Respiratory syncytial virus, Human parvovirus (B 19), Coxsackie viruses types A and B, Echoviruses, Polioviruses, Rhinoviruses, Alastrim (Variola minor virus), Smallpox (Variola major virus), Whitepox Reoviruses, Coltivirus, human Rotavirus, and Orbivirus (Colorado tick fever virus), Rabies virus, Vesicular stomatitis virus, Rubivirus (rubella), Semliki Forest virus, St. Louis encephalitis virus, Venezuelan equine encephalitis virus, Venezuelan equine encephalomyelitis virus, Arenaviruses (a.k.a. South American Hemorrhagic Fever virus), Flexal, Lymphocytic choriomeningitis virus (LCM) (neurotropic strains), Hantaviruses including Hantaan virus, Rift Valley fever virus, Japanese encephalitis virus, Yellow fever virus, Monkeypox virus, Human immunodeficiency virus (HIV) types 1 and 2, Human T cell lymphotropic virus (HTLV) types 1 and 2,

Simian immunodeficiency virus (SIV), Vesicular stomatitis virus, Guanarito virus, Lassa fever virus, Junin virus, Machupo virus, Sabia, Crimean-Congo hemorrhagic fever virus, Ebola viruses, Marburg virus, Tick-borne encephalitis virus complex (flavi) including Central European tick-borne encephalitis, Far Eastern tick-borne encephalitis, Hanzalova, Hypr, Kumlinge, Kyasanur Forest disease, Omsk hemorrhagic fever, and Russian Spring Summer encephalitis viruses,Herpesvirus simiae (Herpes B or Monkey B virus), Cercopithecine herpesvirus 1 (Herpes B virus), Equine morbillivirus (Hendra and Hendra-like viruses), Nipah virus, Variola major virus (Smallpox virus), Variola minor virus (Alastrim), African swine fever virus, African horse sickness virus, Akabane virus, Avian influenza virus (highly pathogenic), Blue tongue virus, Camel pox virus, Classical swine fever virus, Cowdria ruminantium (heartwater), Foot and mouth disease virus, Goat pox virus, Japanese encephalitis virus, Lumpy skin disease virus, Malignant catarrhal fever virus, Menangle virus, Newcastle disease virus (VVND), Vesicular stomatitis virus (exotic), and Zika virus. Antigens encoded by such viruses are known in the art; a peptide epitope suitable for use in a TMMP of the present disclosure can include a peptide from any known viral antigen. In some cases, an HPV antigen is specifically excluded. In some cases, an HBV antigen is specifically excluded.

[00216] In some cases, the epitope peptide present in a TMMP of the present disclosure presents an epitope specific to an HLA-A, -B, -C, -E, -F, or -G allele. In an embodiment, the epitope peptide present in a TMMP presents an epitope restricted to HLA-A*0101, A*0201, A*0301, A*1101, A*2301, A*2402, A*2407, A*3303, and/or A*3401. In an embodiment, the epitope peptide present in a TMMP presents an epitope restricted to HLA- B*0702, B*0801, B*1502, B*3802, B*4001, B*4601, and/or B*5301. In an embodiment, the epitope peptide present in a TMMP presents an epitope restricted to C*0102, C*0303, C*0304, C*0401, C*0602, C*0701, C*702, C*0801, and/or C*1502.

HLA/peptide binding assays

[00217] Whether a given peptide (e.g., a peptide that comprises an epitope) binds a class I HLA (comprising an HLA heavy chain and a β2M polypeptide), and, when bound to the HLA complex, can effectively present an epitope to a TCR, can be determined using any of a number of well-known methods. Assays include binding assays and T-cell activation assays.

Cell-based binding assay

[00218] As one example, a cell-based peptide-induced stabilization assay can be used to determine peptide-HLA class I binding. In this assay, a peptide of interest is allowed to bind to a TAP-deficient cell, i.e., a cell that has defective transporter associated with antigen processing (TAP) machinery, and consequently, few surface class I molecules. Such cells include, e.g., the human T2 cell line (T2 (174 x CEM.T2; American Type Culture Collection (ATCC) No. CRL-1992). Henderson et al. (1992) *Science* 255:1264. Without efficient TAP-mediated transport of cytosolic peptides into the endoplasmic reticulum, assembled class I complexes are structurally unstable, and retained only

transiently at the cell surface. However, when T2 cells are incubated with an exogenous peptide capable of binding class I, surface peptide-HLA class I complexes are stabilized and can be detected by flow cytometry with, e.g., a pan anti-class I monoclonal antibody. The stabilization and resultant increased life-span of peptide-HLA complexes on the cell surface by the addition of a peptide validates their identity. Analysis can be carried out using flow cytometry, e.g., where the pan-HLA class I antibody comprises a fluorescent label. Binding of the peptide to various allelic forms of HLA H chains can be tested by genetically modifying the T2 cells to express an allelic HLA H chain of interest.

[00219] The following is a non-limiting example of use of a T2 assay to assess peptide binding to HLA A*0201. T2 cells are washed in cell culture medium, and concentrated to 10^6 cells/ml. Peptides of interest are prepared in cell culture medium and serially diluted providing concentrations of 200 μM, 100 μM, 20 μM and 2 μM. The cells are mixed 1:1 with each peptide dilution to give a final volume of 200 μL and final peptide concentrations of 100 μM, 50 μM, 10 μM and 1 μM. A HLA A*0201 binding peptide, GILGFVFTL, and a non-HLA A*0201-restricted peptide, HPVGEADYF (HLA-B*3501), are included as positive and negative controls, respectively. The cell/peptide mixtures are kept at 37°C 5% CO_2 for ten minutes; then incubated at room temperature overnight. Cells are then incubated for 2 hours at 37°C and stained with a fluorescently-labeled anti-human HLA antibody. The cells are washed twice with phosphate-buffered saline and analyzed using flow cytometry. The average mean fluorescence intensity (MFI) of the anti-HLA antibody staining is used to measure the strength of binding.

Biochemical binding assay

[00220] HLA polypeptides (HLA heavy chain polypeptide complexed with β2M polypeptide) can be tested for binding to a peptide of interest in a cell-free *in vitro* assay system. For example, a labeled reference peptide (e.g., fluorescently labeled) is allowed to bind to HLA polypeptides (HLA heavy chain polypeptide complexed with β2M polypeptide), to form an HLA-reference peptide complex. The ability of a test peptide of interest to displace the labeled reference peptide from the HLA-reference peptide complex is tested. The relative binding affinity is calculated as the amount of test peptide needed to displace the bound reference peptide. See, e.g., van der Burg et al. (1995) *Human Immunol.* 44:189.

[00221] As another example, a peptide of interest can be incubated with an HLA molecule (HLA heavy chain complexed with a β2M polypeptide), and the stabilization of the HLA/peptide complex can be measured in an immunoassay format. The ability of a peptide of interest to stabilize an HLA molecule is compared to that of a control peptide presenting a known T-cell epitope. Detection of stabilization is based on the presence or absence of the native conformation of the HLA/peptide complex, detected using an anti-HLA antibody. See, e.g., Westrop et al. (2009) *J. Immunol. Methods* 341:76; Steinitz et al. (2012) *Blood* 119:4073; and U.S. Patent No. 9,205,144.

T-cell activation assays

[00222] Whether a given peptide binds a class I HLA (comprising an HLA heavy chain and a β2M polypeptide), and, when bound to the HLA complex, can effectively present an epitope to a TCR, can be determined by assessing T-cell response to the peptide-HLA complex. T-cell responses that can be measured include, e.g., interferon-gamma (IFNγ) production, cytotoxic activity, and the like.

ELISPOT assay

[00223] Suitable assays include, e.g., an enzyme linked immunospot (ELISPOT) assay. In this assay, production of IFNγ by $CD8^+$ T cells is measured following with an antigen-presenting cell (APC) that presents a peptide of interest complexed with HLA class I. Antibody to IFNγ is immobilized on wells of a multi-well plate. APCs are added to the wells, and incubated for a period of time with a peptide of interest, such that the peptide binds HLA class I on the surface of the APCs. $CD8^+$ T cells specific for the peptide are added to the wells, and the plate is incubated for about 24 hours. The wells are then washed, and any IFNγ bound to the immobilized anti-IFNγ antibody is detected using a detectably labeled anti-IFNγ antibody. A colorimetric assay can be used. For example, the detectably labeled anti-IFNγ antibody can be a biotin-labeled anti-IFNγ antibody, which can be detected using, e.g., streptavidin conjugated to alkaline phosphatase. A BCIP/NBT (5-bromo-4-chloro-3-indolyl phosphate/nitro blue tetrazolium) solution is added, to develop the assay. The presence of IFNγ-secreting T cells is identified by colored spots. Negative controls include APCs not contacted with the peptide. APCs expressing various HLA H chain alleles can be used to determine whether a peptide of interest effectively binds to a HLA class I molecule comprising a particular HLA H chain.

Cytotoxicity assays

[00224] Whether a given peptide binds to a particular HLA class I H chain and, when bound to a HLA class I complex comprising the H chain, can effectively present an epitope to a TCR, can also be determined using a cytotoxicity assay. A cytotoxicity assay involves incubation of a target cell with a cytotoxic $CD8^+$ T cell. The target cell displays on its surface a peptide/HLA class I complex comprising a peptide of interest and an HLA class I molecule comprising an HLA H chain to be tested. The target cells can be radioactively labeled, e.g., with ^{51}Cr. Whether the target cell effectively presents an epitope to a TCR on the cytotoxic $CD8^+$ T cell, thereby inducing cytotoxic activity by the $CD8^+$ T cell toward the target cell, is determined by measuring release of ^{51}Cr from the lysed target cell. Specific cytotoxicity can be calculated as the amount of cytotoxic activity in the presence of the peptide minus the amount of cytotoxic activity in the absence of the peptide.

Detection of Antigen-specific T cells with peptide-HLA tetramers

[00225] As another example, multimers (e.g., tetramers) of peptide-HLA complexes are generated with fluorescent or heavy metal tags. The multimers can then be used to identify and quantify specific T cells via flow cytometry (FACS) or mass cytometry (CyTOF). Detection of epitope-specific T cells

provides direct evidence that the peptide-bound HLA molecule is capable of binding to a specific TCR on a subset of antigen-specific T cells. See, e.g., Klenerman et al. (2002) *Nature Reviews Immunol.* 2:263.

Immunomodulatory polypeptides

[00226] In some cases, an immunomodulatory polypeptide present in a TMMP of the present disclosure is a wild-type immunomodulatory polypeptide. In other cases, an immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant immunomodulatory polypeptide that has reduced affinity for a co-immunomodulatory polypeptide, compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the co-immunomodulatory polypeptide. Suitable immunomodulatory domains that exhibit reduced affinity for a co-immunomodulatory domain can have from 1 amino acid (aa) to 20 aa differences from a wild-type immunomodulatory domain. For example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure differs in amino acid sequence by 1 aa, 2 aa, 3 aa, 4 aa, 5 aa, 6 aa, 7 aa, 8 aa, 9 aa, or 10 aa, from a corresponding wild-type immunomodulatory polypeptide. As another example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure differs in amino acid sequence by 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, or 20 aa, from a corresponding wild-type immunomodulatory polypeptide. As an example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acid substitutions, compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes a single amino acid substitution compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 2 amino acid substitutions (e.g., no more than 2 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 3 amino acid substitutions (e.g., no more than 3 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 4 amino acid substitutions (e.g., no more than 4 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 5 amino acid substitutions (e.g., no more than 5 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 6 amino acid substitutions (e.g., no more than 6 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory

polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 7 amino acid substitutions (e.g., no more than 7 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 8 amino acid substitutions (e.g., no more than 8 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 9 amino acid substitutions (e.g., no more than 9 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide. In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 10 amino acid substitutions (e.g., no more than 10 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00227] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 11 amino acid substitutions (e.g., no more than 11 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00228] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 12 amino acid substitutions (e.g., no more than 12 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00229] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 13 amino acid substitutions (e.g., no more than 13 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00230] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 14 amino acid substitutions (e.g., no more than 14 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00231] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 15 amino acid substitutions (e.g., no more than 15 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00232] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 16 amino acid substitutions (e.g., no more than 16 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00233] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 17 amino acid substitutions (e.g., no more than 17 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00234] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 18 amino acid substitutions (e.g., no more than 18 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00235] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 19 amino acid substitutions (e.g., no more than 19 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00236] In some cases, variant immunomodulatory polypeptide present in a TMMP of the present disclosure includes 20 amino acid substitutions (e.g., no more than 20 amino acid substitutions) compared to a corresponding reference (e.g., wild-type) immunomodulatory polypeptide.

[00237] As discussed above, a variant immunomodulatory polypeptide suitable for inclusion in a TMMP of the present disclosure exhibits reduced affinity for a cognate co-immunomodulatory polypeptide, compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide.

[00238] Exemplary pairs of immunomodulatory polypeptide and cognate co-immunomodulatory polypeptide include, but are not limited to:

[00239] a) 4-1BBL (immunomodulatory polypeptide) and 4-1BB (cognate co-immunomodulatory polypeptide);

[00240] b) PD-L1 (immunomodulatory polypeptide) and PD1 (cognate co-immunomodulatory polypeptide);

[00241] c) IL-2 (immunomodulatory polypeptide) and IL-2 receptor (cognate co-immunomodulatory polypeptide);

[00242] d) CD80 (immunomodulatory polypeptide) and CD86 (cognate co-immunomodulatory polypeptide);

[00243] e) CD86 (immunomodulatory polypeptide) and CD28 (cognate co-immunomodulatory polypeptide);

[00244] f) OX40L (CD252) (immunomodulatory polypeptide) and OX40 (CD134) (cognate co-immunomodulatory polypeptide);

[00245] g) Fas ligand (immunomodulatory polypeptide) and Fas (cognate co-immunomodulatory polypeptide);

[00246] h) ICOS-L (immunomodulatory polypeptide) and ICOS (cognate co-immunomodulatory polypeptide);

[00247] i) ICAM (immunomodulatory polypeptide) and LFA-1 (cognate co-immunomodulatory polypeptide);

[00248] j) CD30L (immunomodulatory polypeptide) and CD30 (cognate co-immunomodulatory polypeptide);

[00249] k) CD40 (immunomodulatory polypeptide) and CD40L (cognate co-immunomodulatory polypeptide);

[00250] l) CD83 (immunomodulatory polypeptide) and CD83L (cognate co-immunomodulatory polypeptide);

[00251] m) HVEM (CD270) (immunomodulatory polypeptide) and CD160 (cognate co-immunomodulatory polypeptide);

[00252] n) JAG1 (CD339) (immunomodulatory polypeptide) and Notch (cognate co-immunomodulatory polypeptide);

[00253] o) JAG1 (immunomodulatory polypeptide) and CD46 (cognate co-immunomodulatory polypeptide);

[00254] p) CD80 (immunomodulatory polypeptide) and CTLA4 (cognate co-immunomodulatory polypeptide);

[00255] q) CD86 (immunomodulatory polypeptide) and CTLA4 (cognate co-immunomodulatory polypeptide); and

[00256] r) CD70 (immunomodulatory polypeptide) and CD27 (cognate co-immunomodulatory polypeptide).

[00257] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure has a binding affinity for a cognate co-immunomodulatory polypeptide that is from 100 nM to 100 μM. For example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure has a binding affinity for a cognate co-immunomodulatory polypeptide that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00258] A variant immunomodulatory polypeptide present in a TMMP of the present disclosure exhibits reduced affinity for a cognate co-immunomodulatory polypeptide. Similarly, a TMMP of the present disclosure that comprises a variant immunomodulatory polypeptide exhibits reduced affinity for a cognate co-immunomodulatory polypeptide. Thus, for example, a TMMP of the present disclosure that

comprises a variant immunomodulatory polypeptide has a binding affinity for a cognate co-immunomodulatory polypeptide that is from 100 nM to 100 μM. For example, in some cases, a TMMP of the present disclosure that comprises a variant immunomodulatory polypeptide has a binding affinity for a cognate co-immunomodulatory polypeptide that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00259] As depicted schematically in FIG. 14, an immunomodulatory polypeptide (i.e., one or more immunomodulatory polypeptides) can be present in a TMMP of the present disclosure at any of a variety of positions. FIG. 14 depicts the position of two copies of a variant IL-2 polypeptide; however, the immunomodulatory polypeptide can be any of a variety of immunomodulatory polypeptide, as described herein. As depicted in FIG. 14, an immunomodulatory polypeptide can be: 1) N-terminal to the MHC class I heavy chain; 2) C-terminal to the MHC class I heavy chain and N-terminal to the Ig Fc polypeptide; in other words, between the MHC class I heavy chain and the Ig Fc polypeptide; 3) C-terminal to the Ig Fc polypeptide; 4) N-terminal to the peptide epitope; or 5) C-terminal to the β2M polypeptide.

PD-L1 variants

[00260] As one non-limiting example, in some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant PD-L1 polypeptide. Wild-type PD-L1 binds to PD1.

[00261] A wild-type human PD-L1 polypeptide can comprise the following amino acid sequence: MRIFAVFIFM TYWHLLNAFT VTVPKDLYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR ILVVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVTSTLRIN TTTNEIFYCT FRRLDPEENH TAELVIPGNI LNVSIKICLT LSPST (SEQ ID NO:1).

[00262] A wild-type human PD-L1 ectodomain can comprise the following amino acid sequence: FT VTVPKDLYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR ILVVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVTSTLRIN TTTNEIFYCT FRRLDPEENH TAELVIPGNI LNVSIKI (SEQ ID NO:2).

[00263] A wild-type PD-1 polypeptide can comprise the following amino acid sequence: PGWFLDSPDR PWNPPTFSPA LLVVTEGDNA TFTCSFSNTS ESFVLNWYRM SPSNQTDKLA AFPEDRSQPG QDCRFRVTQL PNGRDFHMSV VRARRNDSGT YLCGAISLAP KAQIKESLRA ELRVTERRAE VPTAHPSPSP RPAGQFQTLV VGVVGGLLGS LVLLVWVLAV ICSRAARGTI GARRTGQPLK EDPSAVPVFS VDYGELDFQW REKTPEPPVP CVPEQTEYAT IVFPSGMGTS SPARRGSADG PRSAQPLRPE DGHCSWPL (SEQ ID NO:3). In some cases, where a TMMP of the present disclosure comprises a variant PD-L1 polypeptide, a "cognate co-immunomodulatory polypeptide" is a PD-1 polypeptide comprising the amino acid sequence of SEQ ID NO:3.

[00264] In some cases, a variant PD-L1 polypeptide exhibits reduced binding affinity to PD-1 (e.g., a PD-1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:3), compared to the binding affinity of a PD-L1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. For example, in some cases, a variant PD-L1 polypeptide of the present disclosure binds PD-1 (e.g., a PD-1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:3) with a binding affinity that is at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of a PD-L1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

[00265] In some cases, a variant PD-L1 polypeptide has a binding affinity to PD-1that is from 1nM to 1mM. In some cases, a variant PD-L1 polypeptide of the present disclosure has a binding affinity to PD-1 that is from 100 nM to 100 μM. As another example, in some cases, a variant PD-L1 polypeptide has a binding affinity for PD1 (e.g., a PD1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:3) that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00266] In some cases, a variant PD-L1 polypeptide has a single amino acid substitution compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has from 2 to 10 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 2 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or

SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 3 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 4 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 5 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 6 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 7 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 8 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 9 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2. In some cases, a variant PD-L1 polypeptide has 10 amino acid substitutions compared to the PD-L1 amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

[00267] A suitable PD-L1 variant includes a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:

[00268] FT VTVPK**X**LYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR ILVVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVTSTLRIN TTTNEIFYCT FRRLDPEENH TAELVIPGNI LNVSIKI (SEQ ID NO: 52), where X is any amino acid other than Asp. In some cases, X is Ala. In some cases, X is Arg.

[00269] A suitable PD-L1 variant includes a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:

[00270] FT VTVPKDLYVV EYGSNMTIEC KFPVEKQLDL AAL**X**VYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR ILVVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVTSTLRIN TTTNEIFYCT FRRLDPEENH TAELVIPGNI LNVSIKI (SEQ ID NO: 53), where X is any amino acid other than Ile. In some cases, X is Asp.

[00271] A suitable PD-L1 variant includes a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following amino acid sequence:

[00272] FT VTVPKDLYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG E**X**DLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV

NAPYNKINQR ILVVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVTSTLRIN TTTNEIFYCT FRRLDPEENH TAELVIPGNI LNVSIKI (SEQ ID NO:54), where X is any amino acid other than Glu. In some cases, X is Arg.

CD80 variants

[00273] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant CD80 polypeptide. Wild-type CD80 binds to CD28. Wild-type CD80 also binds to CD86.

[00274] A wild-type amino acid sequence of the ectodomain of human CD80 can be as follows:

[00275] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:4).

[00276] A wild-type CD28 amino acid sequence can be as follows: MLRLLLALNL FPSIQVTGNK ILVKQSPMLV AYDNAVNLSC KYSYNLFSRE FRASLHKGLD SAVEVCVVYG NYSQQLQVYS KTGFNCDGKL GNESVTFYLQ NLYVNQTDIY FCKIEVMYPP PYLDNEKSNG TIIHVKGKHL CPSPLFPGPS KPFWVLVVVG GVLACYSLLV TVAFIIFWVR SKRSRLLHSD YMNMTPRRPG PTRKHYQPYA PPRDFAAYRS (SEQ ID NO:5). In some cases, where a TMMP of the present disclosure comprises a variant CD80 polypeptide, a "cognate co-immunomodulatory polypeptide" is a CD28 polypeptide comprising the amino acid sequence of SEQ ID NO:5.

[00277] A wild-type CD28 amino acid sequence can be as follows: MLRLLLALNL FPSIQVTGNK ILVKQSPMLV AYDNAVNLSW KHLCPSPLFP GPSKPFWVLV VVGGVLACYS LLVTVAFIIF WVRSKRSRLL HSDYMNMTPR RPGPTRKHYQ PYAPPRDFAA YRS (SEQ ID NO:6)

[00278] A wild-type CD28 amino acid sequence can be as follows: MLRLLLALNL FPSIQVTGKH LCPSPLFPGP SKPFWVLVVV GGVLACYSLL VTVAFIIFWV RSKRSRLLHS DYMNMTPRRP GPTRKHYQPY APPRDFAAYR S (SEQ ID NO:7).

[00279] In some cases, a variant CD80 polypeptide exhibits reduced binding affinity to CD28, compared to the binding affinity of a CD80 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:4 for CD28. For example, in some cases, a variant CD80 polypeptide binds CD28 with a binding affinity that is at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of a CD80 polypeptide comprising the amino acid

sequence set forth in SEQ ID NO:4 for CD28 (e.g., a CD28 polypeptide comprising the amino acid sequence set forth in one of SEQ ID NO:5, 6, or 7).

[00280] In some cases, a variant CD80 polypeptide has a binding affinity to CD28 that is from 100 nM to 100 μM. As another example, in some cases, a variant CD80 polypeptide of the present disclosure has a binding affinity for CD28 (e.g., a CD28 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:5, SEQ ID NO:6, or SEQ ID NO:7) that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00281] In some cases, a variant CD80 polypeptide has a single amino acid substitution compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has from 2 to 10 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 2 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 3 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 4 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 5 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 6 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 7 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 8 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 9 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4. In some cases, a variant CD80 polypeptide has 10 amino acid substitutions compared to the CD80 amino acid sequence set forth in SEQ ID NO:4.

[00282] Suitable CD80 variants include a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to any one of the following amino acid sequences:

[00283] VIHVTK EVKEVATLSC GH**X**VSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV

SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO: 55), where X is any amino acid other than Asn. In some cases, X is Ala;

[00284] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDIT**X**NLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO: 56), where X is any amino acid other than Asn. In some cases, X is Ala;

[00285] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS **X**VILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:57), where X is any amino acid other than Ile. In some cases, X is Ala;

[00286] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVL**X** YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:58), where X is any amino acid other than Lys. In some cases, X is Ala;

[00287] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS **X**DPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:60), where X is any amino acid other than Gln. In some cases, X is Ala;

[00288] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS Q**X**PETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:61), where X is any amino acid other than Asp. In some cases, X is Ala;

[00289] VIHVTK EVKEVATLSC GHNVSVEE**X**A QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:62), where X is any amino acid other than Leu. In some cases, X is Ala;

[00290] VIHVTK EVKEVATLSC GHNVSVEELA QTRI**X**WQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA

DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:63), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00291] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYW**X**KEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:64), where X is any amino acid other than Gln. In some cases, X is Ala;

[00292] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK K**X**VLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:65), where X is any amino acid other than Met. In some cases, X is Ala;

[00293] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KM**X**LTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:66), where X is any amino acid other than Val. In some cases, X is Ala;

[00294] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MN**X**WPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:67), where X is any amino acid other than Ile. In some cases, X is Ala;

[00295] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPE**X**KNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:68), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00296] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIF**X**ITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:69), where X is any amino acid other than Asp. In some cases, X is Ala;

[00297] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA D**X**PTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:70), where X is any amino acid other than Phe. In some cases, X is Ala;

[00298] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTV**X** QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:71), where X is any amino acid other than Ser. In some cases, X is Ala; and

[00299] VIHVTK EVKEVATLSC GHNVSVEELA QTRIYWQKEK KMVLTMMSGD MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH LAEVTLSVKA DFPT**X**SISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN WNTTKQEHFP DN (SEQ ID NO:72), where X is any amino acid other than Pro. In some cases, X is Ala.

CD86 variants

[00300] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant CD86 polypeptide. Wild-type CD86 binds to CD28. In some cases, where a TMMP of the present disclosure comprises a variant CD86 polypeptide, a "cognate co-immunomodulatory polypeptide" is a CD28 polypeptide comprising the amino acid sequence of SEQ ID NO:5.

[00301] The amino acid sequence of the full ectodomain of a wild-type human CD86 can be as follows:

APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM**N**RTSF**D**SDS**W**
TLRLHNLQIKDKGLYQCIIH**H**KKPTGMIRIHQMNSELSV**L**ANFSQPEIVPISNITENVYINLTCSSIHGY
PEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETDKTRLLSSPFS
IELEDPQPPPDHIP (SEQ ID NO:8).

[00302] The amino acid sequence of the IgV domain of a wild-type human CD86 can be as follows:

APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM**N**RTSF**D**SDS**W**
TLRLHNLQIKDKGLYQCIIH**H**KKPTGMIRIHQMNSELSVL (SEQ ID NO:9).

[00303] In some cases, a variant CD86 polypeptide exhibits reduced binding affinity to CD28, compared to the binding affinity of a CD86 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:8 or SEQ ID NO:9 for CD28. For example, in some cases, a variant CD86 polypeptide

binds CD28 with a binding affinity that is at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of a CD86 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:8 or SEQ ID NO:9 for CD28 (e.g., a CD28 polypeptide comprising the amino acid sequence set forth in one of SEQ ID NO:5, 6, or 7).

[00304] In some cases, a variant CD86 polypeptide has a binding affinity to CD28 that is from 100 nM to 100 μM. As another example, in some cases, a variant CD86 polypeptide of the present disclosure has a binding affinity for CD28 (e.g., a CD28 polypeptide comprising the amino acid sequence set forth in one of SEQ ID NOs:5, 6, or 7) that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00305] In some cases, a variant CD86 polypeptide has a single amino acid substitution compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has from 2 to 10 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 2 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 3 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 4 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 5 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 6 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 7 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 8 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 9 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8. In some cases, a variant CD86 polypeptide has 10 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:8.

[00306] In some cases, a variant CD86 polypeptide has a single amino acid substitution compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide

has from 2 to 10 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 2 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 3 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 4 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 5 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 6 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 7 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 8 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 9 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9. In some cases, a variant CD86 polypeptide has 10 amino acid substitutions compared to the CD86 amino acid sequence set forth in SEQ ID NO:9.

[00307] Suitable CD86 variants include a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to any one of the following amino acid sequences:

[00308] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM **X**RTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:73), where X is any amino acid other than Asn. In some cases, X is Ala;

[00309] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSF**X**SDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:74), where X is any amino acid other than Asp. In some cases, X is Ala;

[00310] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSFDSDS**X**TLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:75), where X is any amino acid other than Trp. In some cases, X is Ala;

[00311] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSFDSDSWTLRLHNLQIKDKGLYQCIIH**X**KKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI

NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD
KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:76), where X is any amino acid other than His. In some cases, X is Ala;

[00312] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM
XRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:77), where X is any amino acid other than Asn. In some cases, X is Ala;

[00313] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM
NRTSF**X**SDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:78), where X is any amino acid other than Asp. In some cases, X is Ala;

[00314] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDS**X**TLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:79), where X is any amino acid other than Trp. In some cases, X is Ala;

[00315] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIH**X**KKPTGMIRIHQMNSELSVL (SEQ ID NO:80), where X is any amino acid other than His. In some cases, X is Ala;

[00316] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENL**X**LNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI
NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD
KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:81), where X is any amino acid other than Val. In some cases, X is Ala;

[00317] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENL**X**LNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:82), where X is any amino acid other than Val. In some cases, X is Ala;

[00318] APLKIQAYFNETADLPCQFANSQNQSLSELVVFW**X**DQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI
NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD
KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:83), where X is any amino acid other than Gln. In some cases, X is Ala;

[00319] APLKIQAYFNETADLPCQFANSQNQSLSELVVFW**X**DQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:84), where X is any amino acid other than Gln. In some cases, X is Ala;

[00320] APLKIQAYFNETADLPCQFANSQNQSLSELVV**X**WQDQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI
NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD

KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:85), where X is any amino acid other than Phe. In some cases, X is Ala;

[00321] APLKIQAYFNETADLPCQFANSQNQSLSELVV**X**WQDQENLVLNEVYLGKEKFDSVHSKYM NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:86), where X is any amino acid other than Phe. In some cases, X is Ala;

[00322] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSFDSDSWT**X**RLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:87), where X is any amino acid other than Leu. In some cases, X is Ala;

[00323] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSFDSDSWT**X**RLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:88), where X is any amino acid other than Leu. In some cases, X is Ala;

[00324] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSK**X**M NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:89), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00325] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSK**X**M NRTSFDSDSWTLRLHNLQIKDKGLYQCIIHHKKPTGMIRIHQMNSELSVL (SEQ ID NO:90), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00326] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM **X**RTSFDSDSWTLRLHNLQIKDKGLYQCIIH**X**KKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVYI NLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILETD KTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:91), where the first X is any amino acid other than Asn and the second X is any amino acid other than His. In some cases, the first and the second X are both Ala;

[00327] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM **X**RTSFDSDSWTLRLHNLQIKDKGLYQCIIH**X**KKPTGMIRIHQMNSELSVL (SEQ ID NO:92), where the first X is any amino acid other than Asn and the second X is any amino acid other than His. In some cases, the first and the second X are both Ala;

[00328] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSF**X_1**SDSWTLRLHNLQIKDKGLYQCIIH**X_2**KKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENVY INLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILET

DKTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:93), where X_1 is any amino acid other than Asp, and X_2 is any amino acid other than His . In some cases, X_1 is Ala and X_2 is Ala;

[00329] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM NRTSF**X_1**SDSWTLRLHNLQIKDKGLYQCIIH**X_2**KKPTGMIRIHQMNSELSVL (SEQ ID NO:94), where the first X is any amino acid other than Asn and the second X is any amino acid other than His. In some cases, the first and the second X are both Ala;

[00330] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM **X_1**RTSF**X_2**SDSWTLRLHNLQIKDKGLYQCIIH**X_3**KKPTGMIRIHQMNSELSVLANFSQPEIVPISNITENV YINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISLSVSFPDVTSNMTIFCILE TDKTRLLSSPFSIELEDPQPPPDHIP (SEQ ID NO:95), where X_1 is any amino acid other than Asn, X_2 is any amino acid other than Asp, and X_3 is any amino acid other than His . In some cases, X_1 is Ala, X_2 is Ala, and X_3 is Ala; and

[00331] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWQDQENLVLNEVYLGKEKFDSVHSKYM **X_1**RTSF**X_2**SDSWTLRLHNLQIKDKGLYQCIIH**X_3**KKPTGMIRIHQMNSELSVL (SEQ ID NO:96), where X_1 is any amino acid other than Asn, X_2 is any amino acid other than Asp, and X_3 is any amino acid other than His . In some cases, X_1 is Ala, X_2 is Ala, and X_3 is Ala.

4-1BBL variants

[00332] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant 4-1BBL polypeptide. Wild-type 4-1BBL binds to 4-1BB (CD137).

[00333] A wild-type 4-1BBL amino acid sequence can be as follows: MEYASDASLD PEAPWPPAPR ARACRVLPWA LVAGLLLLLL LAAACAVFLA CPWAVSGARA SPGSAASPRL REGPELSPDD PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:10).

[00334] In some cases, a variant 4-1BBL polypeptide is a variant of the tumor necrosis factor (TNF) homology domain (THD) of human 4-1BBL.

[00335] A wild-type amino acid sequence of the THD of human 4-1BBL can be, e.g., one of SEQ ID NOs:11-13, as follows:

[00336] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:11).

[00337] D PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:12).

[00338] D PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPA (SEQ ID NO:13).

[00339] A wild-type 4-1BB amino acid sequence can be as follows: MGNSCYNIVA TLLLVLNFER TRSLQDPCSN CPAGTFCDNN RNQICSPCPP NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS MCEQDCKQGQ ELTKKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG TKERDVVCGP SPADLSPGAS SVTPPAPARE PGHSPQIISF FLALTSTALL FLLFFLTLRF SVVKRGRKKL LYIFKQPFMR PVQTTQEEDG CSCRFPEEEE GGCEL (SEQ ID NO:14). In some cases, where a TMMP of the present disclosure comprises a variant 4-1BBL polypeptide, a "cognate co-immunomodulatory polypeptide" is a 4-1BB polypeptide comprising the amino acid sequence of SEQ ID NO:14.

[00340] In some cases, a variant 4-1BBL polypeptide exhibits reduced binding affinity to 4-1BB, compared to the binding affinity of a 4-1BBL polypeptide comprising the amino acid sequence set forth in one of SEQ ID NOs:10-13. For example, in some cases, a variant 4-1BBL polypeptide of the present disclosure binds 4-1BB with a binding affinity that is at least 10% less, at least 15% less, at least 20% less, at least 25%, at least 30% less, at least 35% less, at least 40% less, at least 45% less, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of a 4-1BBL polypeptide comprising the amino acid sequence set forth in one of SEQ ID NOs:10-13 for a 4-1BB polypeptide (e.g., a 4-1BB polypeptide comprising the amino acid sequence set forth in SEQ ID NO:14), when assayed under the same conditions.

[00341] In some cases, a variant 4-1BBL polypeptide has a binding affinity to 4-1BB that is from 100 nM to 100 μM. As another example, in some cases, a variant 4-1BBL polypeptide has a binding affinity for 4-1BB (e.g., a 4-1BB polypeptide comprising the amino acid sequence set forth in SEQ ID NO:14) that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10

μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00342] In some cases, a variant 4-1BBL polypeptide has a single amino acid substitution compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has from 2 to 10 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 2 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 3 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 4 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 5 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 6 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 7 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 8 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 9 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13. In some cases, a variant 4-1BBL polypeptide has 10 amino acid substitutions compared to the 4-1BBL amino acid sequence set forth in one of SEQ ID NOs:10-13.

[00343] Suitable 4-1BBL variants include a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to any one of the following amino acid sequences:

[00344] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSY**X**EDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO: 97), where X is any amino acid other than Lys. In some cases, X is Ala;

[00345] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAW**X**LTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO: 98), where X is any amino acid other than Gln. In some cases, X is Ala;

[00346] PAGLLDLRQG **X**FAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS

EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO: 99), where X is any amino acid other than Met. In some cases, X is Ala;

[00347] PAGLLDLRQG M**X**AQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO: 100), where X is any amino acid other than Phe. In some cases, X is Ala;

[00348] PAGLLDLRQG MFA**X**LVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:101), where X is any amino acid other than Gln. In some cases, X is Ala;

[00349] PAGLLDLRQG MFAQ**X**VAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:102), where X is any amino acid other than Leu. In some cases, X is Ala;

[00350] PAGLLDLRQG MFAQL**X**AQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:103), where X is any amino acid other than Val. In some cases, X is Ala;

[00351] PAGLLDLRQG MFAQLVA**X**NV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:104), where X is any amino acid other than Gln. In some cases, X is Ala;

[00352] PAGLLDLRQG MFAQLVAQ**X**V LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:105), where X is any amino acid other than Asn. In some cases, X is Ala;

[00353] PAGLLDLRQG MFAQLVAQN**X** LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:106), where X is any amino acid other than Val. In some cases, X is Ala;

[00354] PAGLLDLRQG MFAQLVAQNV **X**LIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:107), where X is any amino acid other than Leu. In some cases, X is Ala;

[00355] PAGLLDLRQG MFAQLVAQNV L**X**IDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:108), where X is any amino acid other than Leu. In some cases, X is Ala;

[00356] PAGLLDLRQG MFAQLVAQNV LL**X**DGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:109), where X is any amino acid other than Ile. In some cases, X is Ala;

[00357] PAGLLDLRQG MFAQLVAQNV LLI**X**GPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:110), where X is any amino acid other than Asp. In some cases, X is Ala;

[00358] PAGLLDLRQG MFAQLVAQNV LLID**X**PLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:111), where X is any amino acid other than Gly. In some cases, X is Ala;

[00359] PAGLLDLRQG MFAQLVAQNV LLIGG**X**LSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:112), where X is any amino acid other than Pro. In some cases, X is Ala;

[00360] PAGLLDLRQG MFAQLVAQNV LLIGGP**X**SWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:113), where X is any amino acid other than Leu. In some cases, X is Ala;

[00361] PAGLLDLRQG MFAQLVAQNV LLIGGPL**X**WY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:114), where X is any amino acid other than Ser. In some cases, X is Ala;

[00362] PAGLLDLRQG MFAQLVAQNV LLIGGPLS**X**Y SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:115), where X is any amino acid other than Trp. In some cases, X is Ala;

[00363] PAGLLDLRQG MFAQLVAQNV LLIGGPLSW**X** SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS

EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:116), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00364] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY **X**DPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:117), where X is any amino acid other than Ser. In some cases, X is Ala;

[00365] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY S**X**PGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:118), where X is any amino acid other than Asp. In some cases, X is Ala;

[00366] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SD**X**GLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:119), where X is any amino acid other than Pro. In some cases, X is Ala;

[00367] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDP**X**LAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:120), where X is any amino acid other than Gly. In some cases, X is Ala;

[00368] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPG**X**AGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:121), where X is any amino acid other than Leu. In some cases, X is Ala;

[00369] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLA**X**VSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:122), where X is any amino acid other than Gly. In some cases, X is Ala;

[00370] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAG**X**SL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:123), where X is any amino acid other than Val. In some cases, X is Ala;

[00371] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGV**X**L TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:124), where X is any amino acid other than Ser. In some cases, X is Ala;

[00372] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVS**X** TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:125), where X is any amino acid other than Leu. In some cases, X is Ala;

[00373] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL **X**GGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:126), where X is any amino acid other than Thr. In some cases, X is Ala;

[00374] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL T**X**GLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:127), where X is any amino acid other than Gly. In some cases, X is Ala;

[00375] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TG**X**LSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:128), where X is any amino acid other than Gly. In some cases, X is Ala;

[00376] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGG**X**SYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:129), where X is any amino acid other than Leu. In some cases, X is Ala;

[00377] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGL**X**YKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:130), where X is any amino acid other than Ser. In some cases, X is Ala;

[00378] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLS**X**KEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:131), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00379] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYK**X**DT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:132), where X is any amino acid other than Glu. In some cases, X is Ala;

[00380] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKE**X**T KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS

EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:133), where X is any amino acid other than Asp. In some cases, X is Ala;

[00381] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKED**X** KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:134), where X is any amino acid other than Thr. In some cases, X is Ala;

[00382] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT **X**ELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:135), where X is any amino acid other than Lys. In some cases, X is Ala;

[00383] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT K**X**LVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:136), where X is any amino acid other than Glu. In some cases, X is Ala;

[00384] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYV**X**FQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:137), where X is any amino acid other than Phe. In some cases, X is Ala;

[00385] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVF**X**QLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:138), where X is any amino acid other than Phe. In some cases, X is Ala;

[00386] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFF**X**LELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:139), where X is any amino acid other than Gln. In some cases, X is Ala;

[00387] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQ**X**ELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:140), where X is any amino acid other than Leu. In some cases, X is Ala;

[00388] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQL**X**LR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:141), where X is any amino acid other than Glu. In some cases, X is Ala;

[00389] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLE**X**R RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:142), where X is any amino acid other than Leu. In some cases, X is Ala;

[00390] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLEL**X** RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:143), where X is any amino acid other than Arg. In some cases, X is Ala;

[00391] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR **X**VVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:144), where X is any amino acid other than Arg. In some cases, X is Ala;

[00392] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR R**X**VAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:145), where X is any amino acid other than Val. In some cases, X is Ala;

[00393] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RV**X**AGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:146), where X is any amino acid other than Val. In some cases, X is Ala;

[00394] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVA**X**EGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:147), where X is any amino acid other than Gly. In some cases, X is Ala;

[00395] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAG**X**GSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:148), where X is any amino acid other than Glu. In some cases, X is Ala;

[00396] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGE**X**SGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:149), where X is any amino acid other than Gly. In some cases, X is Ala;

[00397] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEG**X**GS VSLALHLQPL RSAAGAAALA LTVDLPPASS

EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:150), where X is any amino acid other than Ser. In some cases, X is Ala;

[00398] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTV**X**LPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:151), where X is any amino acid other than Asp. In some cases, X is Ala;

[00399] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVD**X**PPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:152), where X is any amino acid other than Leu. In some cases, X is Ala;

[00400] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDL**X**PASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:153), where X is any amino acid other than Pro. In some cases, X is Ala;

[00401] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPA**X**S EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:154), where X is any amino acid other than Ser. In some cases, X is Ala;

[00402] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPAS**X** EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:155), where X is any amino acid other than Ser. In some cases, X is Ala;

[00403] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS **X**ARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:156), where X is any amino acid other than Glu. In some cases, X is Ala;

[00404] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EA**X**NSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:157), where X is any amino acid other than Arg. In some cases, X is Ala;

[00405] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EAR**X**SAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:158), where X is any amino acid other than Asn. In some cases, X is Ala;

[00406] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARN**X**AFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:159), where X is any amino acid other than Ser. In some cases, X is Ala;

[00407] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSA**X**GFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:160), where X is any amino acid other than Phe. In some cases, X is Ala;

[00408] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAG**X** RLGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:161), where X is any amino acid other than Gln. In some cases, X is Ala;

[00409] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ **X**LGVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:162), where X is any amino acid other than Arg. In some cases, X is Ala;

[00410] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ R**X**GVHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:163), where X is any amino acid other than Leu. In some cases, X is Ala;

[00411] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RL**X**VHLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:164), where X is any amino acid other than Gly. In some cases, X is Ala;

[00412] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG**X**HLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:165), where X is any amino acid other than Val. In some cases, X is Ala;

[00413] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGV**X**LHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:166), where X is any amino acid other than His. In some cases, X is Ala;

[00414] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS

EARNSAFGFQ GRLLHLSAGQ RLGVH**X**HTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:167), where X is any amino acid other than Leu. In some cases, X is Ala;

[00415] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHL**X**TEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:168), where X is any amino acid other than His. In some cases, X is Ala;

[00416] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLH**X**EA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:169), where X is any amino acid other than Thr. In some cases, X is Ala;

[00417] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHT**X**A RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:170), where X is any amino acid other than Glu. In some cases, X is Ala;

[00418] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA **X**ARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:171), where X is any amino acid other than Arg. In some cases, X is Ala;

[00419] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RA**X**HAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:172), where X is any amino acid other than Arg. In some cases, X is Ala;

[00420] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RAR**X**AWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:173), where X is any amino acid other than His. In some cases, X is Ala;

[00421] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHA**X**QLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:174), where X is any amino acid other than Trp. In some cases, X is Ala;

[00422] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQ**X**TQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:175), where X is any amino acid other than Leu. In some cases, X is Ala;

[00423] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQL**X**Q GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:176), where X is any amino acid other than Thr. In some cases, X is Ala;

[00424] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLT**X** GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:177), where X is any amino acid other than Gln. In some cases, X is Ala;

[00425] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ **X**ATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:178), where X is any amino acid other than Gly. In some cases, X is Ala;

[00426] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GA**X**VLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:179), where X is any amino acid other than Thr. In some cases, X is Ala; and

[00427] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ GAT**X**LGLFRV TPEIPAGLPS PRSE (SEQ ID NO:180), where X is any amino acid other than Val. In some cases, X is Ala.

IL-2 variants

[00428] In some cases, a variant immunomodulatory polypeptide present in a TMMP of the present disclosure is a variant IL-2 polypeptide. Wild-type IL-2 binds to IL-2 receptor (IL-2R), i.e., a heterotrimeric polypeptide comprising IL-2Rα, IL-2Rβ, and IL-2Rγ.

[00429] A wild-type IL-2 amino acid sequence can be as follows: APTSSSTKKT QLQL**EH**LLL**D** LQMILNGINN YKNPKLTRML T**F**KF**Y**MPKKA TELKHLQCLEEELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNRWITFC**Q**SIIS TLT (SEQ ID NO:15).

[00430] Wild-type IL2 binds to an IL2 receptor (IL2R) on the surface of a cell. An IL2 receptor is in some cases a heterotrimeric polypeptide comprising an alpha chain (IL-2Rα; also referred to as CD25), a beta chain (IL-2Rβ; also referred to as CD122: and a gamma chain (IL-2Rγ; also referred to as CD132). Amino acid sequences of human IL-2Rα, IL2Rβ, and IL-2Rγ can be as follows.

[00431] Human IL-2Rα: ELCDDDPPE IPHATFKAMA YKEGTMLNCE CKRGFRRIKS GSLYMLCTGN SSHSSWDNQC QCTSSATRNT TKQVTPQPEE QKERKTTEMQ SPMQPVDQAS

LPGHCREPPP WENEATERIY HFVVGQMVYY QCVQGYRALH RGPAESVCKM THGKTRWTQP QLICTGEMET SQFPGEEKPQ ASPEGRPESE TSCLVTTTDF QIQTEMAATM ETSIFTTEYQ VAVAGCVFLL ISVLLLSGLT WQRRQRKSRR TI (SEQ ID NO:16).

[00432] Human IL-2Rβ: VNG TSQFTCFYNS RANISCVWSQ DGALQDTSCQ VHAWPDRRRW NQTCELLPVS QASWACNLIL GAPDSQKLTT VDIVTLRVLC REGVRWRVMA IQDFKPFENL RLMAPISLQV VHVETHRCNI SWEISQASHY FERHLEFEAR TLSPGHTWEE APLLTLKQKQ EWICLETLTP DTQYEFQVRV KPLQGEFTTW SPWSQPLAFR TKPAALGKDT IPWLGHLLVG LSGAFGFIIL VYLLINCRNT GPWLKKVLKC NTPDPSKFFS QLSSEHGGDV QKWLSSPFPS SSFSPGGLAP EISPLEVLER DKVTQLLLQQ DKVPEPASLS SNHSLTSCFT NQGYFFFHLP DALEIEACQV YFTYDPYSEE DPDEGVAGAP TGSSPQPLQP LSGEDDAYCT FPSRDDLLLF SPSLLGGPSP PSTAPGGSGA GEERMPPSLQ ERVPRDWDPQ PLGPPTPGVP DLVDFQPPPE LVLREAGEEV PDAGPREGVS FPWSRPPGQG EFRALNARLP LNTDAYLSLQ ELQGQDPTHL V (SEQ ID NO:17).

[00433] Human IL-2Rγ: LNTTILTP NGNEDTTADF FLTTMPTDSL SVSTLPLPEV QCFVFNVEYM NCTWNSSSEP QPTNLTLHYW YKNSDNDKVQ KCSHYLFSEE ITSGCQLQKK EIHLYQTFVV QLQDPREPRR QATQMLKLQN LVIPWAPENL TLHKLSESQL ELNWNNRFLN HCLEHLVQYR TDWDHSWTEQ SVDYRHKFSL PSVDGQKRYT FRVRSRFNPL CGSAQHWSEW SHPIHWGSNT SKENPFLFAL EAVVISVGSM GLIISLLCVY FWLERTMPRI PTLKNLEDLV TEYHGNFSAW SGVSKGLAES LQPDYSERLC LVSEIPPKGG ALGEGPGASP CNQHSPYWAP PCYTLKPET (SEQ ID NO:18).

[00434] In some cases, where a TMMP of the present disclosure comprises a variant IL-2 polypeptide, a "cognate co-immunomodulatory polypeptide" is an IL-2R comprising polypeptides comprising the amino acid sequences of SEQ ID NO:16, 17, and 18.

[00435] In some cases, a variant IL-2 polypeptide exhibits reduced binding affinity to IL-2R, compared to the binding affinity of a IL-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:15. For example, in some cases, a variant IL-2 polypeptide binds IL-2R with a binding affinity that is at least 10% less, at least 15% less, at least 20% less, at least 25%, at least 30% less, at least 35% less, at least 40% less, at least 45% less, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of an IL-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:15 for an IL-2R (e.g., an IL-2R comprising polypeptides comprising the amino acid sequence set forth in SEQ ID NOs:16-18), when assayed under the same conditions.

[00436] In some cases, a variant IL-2 polypeptide has a binding affinity to IL-2R that is from 100 nM to 100 μM. As another example, in some cases, a variant IL-2 polypeptide has a binding affinity for IL-2R (e.g., an IL-2R comprising polypeptides comprising the amino acid sequence set forth in SEQ ID NOs:16-18) that is from about 100 nM to 150 nM, from about 150 nM to about 200 nM, from about 200 nM to about 250 nM, from about 250 nM to about 300 nM, from about 300 nM to about 350 nM, from about 350 nM to about 400 nM, from about 400 nM to about 500 nM, from about 500 nM to about 600 nM, from about 600 nM to about 700 nM, from about 700 nM to about 800 nM, from about 800 nM to about 900 nM, from about 900 nM to about 1 μM, to about 1 μM to about 5 μM, from about 5 μM to about 10 μM, from about 10 μM to about 15 μM, from about 15 μM to about 20 μM, from about 20 μM to about 25 μM, from about 25 μM to about 50 μM, from about 50 μM to about 75 μM, or from about 75 μM to about 100 μM.

[00437] In some cases, a variant IL-2 polypeptide has a single amino acid substitution compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has from 2 to 10 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 2 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 3 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 4 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 5 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 6 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 7 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 8 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 9 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15. In some cases, a variant IL-2 polypeptide has 10 amino acid substitutions compared to the IL-2 amino acid sequence set forth in SEQ ID NO:15.

[00438] Suitable IL-2 variants include a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to any one of the following amino acid sequences:

[00439] APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML T**X**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:181), where X is any amino acid other than Phe. In some cases, X is Ala. In some cases, X is Met. In some cases, X is Pro. In some cases, X is Ser. In some

cases, X is Thr. In some cases, X is Trp. In some cases, X is Tyr. In some cases, X is Val. In some cases, X is His;

[00440] APTSSSTKKT QLQLEHLLL**X** LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:182), where X is any amino acid other than Asp. In some cases, X is Ala;

[00441] APTSSSTKKT QLQL**X**HLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:183), where X is any amino acid other than Glu. In some cases, X is Ala.

[00442] APTSSSTKKT QLQLE**X**LLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:184), where X is any amino acid other than His. In some cases, X is Ala. In some cases, X is Thr. In some cases, X is Asn. In some cases, X is Cys. In some cases, X is Gln. In some cases, X is Met. In some cases, X is Val. In some cases, X is Trp;

[00443] APTSSSTKKT QLQLE**X**LLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:185), where X is any amino acid other than His. In some cases, X is Ala. In some cases, X is Arg. In some cases, X is Asn. In some cases, X is Asp. In some cases, X is Cys. In some cases, X is Glu. In some cases, X is Gln. In some cases, X is Gly. In some cases, X is Ile. I n some cases, X is Lys. In some cases, X is Leu. In some cases, X is Met. In some cases, X is Phe. In some cases, X is Pro. In some cases, X is Ser. In some cases, X is Thr. In some cases, X is Tyr. In some cases, X is Trp. In some cases, X is Val;

[00444] APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKF**X**MPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:186), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00445] APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFC**X**SIIS TLT (SEQ ID NO:187), where X is any amino acid other than Gln. In some cases, X is Ala;

[00446] APTSSSTKKT QLQLE$\mathbf{X_1}$LLLD LQMILNGINN YKNPKLTRML T$\mathbf{X_2}$KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:188), where X_1 is any amino acid other than His, and

where X_2 is any amino acid other than Phe. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_1 is Ala; and X_2 is Ala. In some cases, X_1 is Thr; and X_2 is Ala;

[00447] APTSSSTKKT QLQLEHLLL**X1** LQMILNGINN YKNPKLTRML T**X2**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:189), where X_1 is any amino acid other than Asp; and where X_2 is any amino acid other than Phe. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_1 is Ala; and X_2 is Ala;

[00448] APTSSSTKKT QLQL**X1**HLLL**X2** LQMILNGINN YKNPKLTRML T**X3**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:190), where X_1 is any amino acid other than Glu; where X_2 is any amino acid other than Asp; and where X_3 is any amino acid other than Phe. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_1 is Ala; X_2 is Ala; and X_3 is Ala;

[00449] APTSSSTKKT QLQLE**X1**LLL**X2** LQMILNGINN YKNPKLTRML T**X3**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:191), where X_1 is any amino acid other than His; where X_2 is any amino acid other than Asp; and where X_3 is any amino acid other than Phe. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_1 is Ala; X_2 is Ala; and X_3 is Ala;

[00450] APTSSSTKKT QLQLEHLLL**X1** LQMILNGINN YKNPKLTRML T**X2**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFC**X3**SIIS TLT (SEQ ID NO:192), where X_1 is any amino acid other than Asp; where X_2 is any amino acid other than Phe; and where X_3 is any amino acid other than Gln. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_1 is Ala; X_2 is Ala; and X_3 is Ala;

[00451] APTSSSTKKT QLQLEHLLL**X1** LQMILNGINN YKNPKLTRML T**X2**KF**X3**MPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:193), where X_1 is any amino acid other than Asp; where X_2 is any amino acid other than Phe; and where X_3 is any amino acid other than Tyr. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_1 is Ala; X_2 is Ala; and X_3 is Ala;

[00452] APTSSSTKKT QLQLE**X1**LLL**X2** LQMILNGINN YKNPKLTRML T**X3**KF**X4**MPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:194), where X_1 is any amino acid other than His;

where X_2 is any amino acid other than Asp; where X_3 is any amino acid other than Phe; and where X_4 is any amino acid other than Tyr. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_4 is Ala. In some cases, X_1 is Ala; X_2 is Ala; X_3 is Ala; and X_4 is Ala;

[00453] APTSSSTKKT QLQLEHLLL**X_1** LQMILNGINN YKNPKLTRML T**X_2**KF**X_3**MPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFC**X_4**SIIS TLT (SEQ ID NO:195), where X_1 is any amino acid other than Asp; where X_2 is any amino acid other than Phe; where X_3 is any amino acid other than Tyr; and where X_4 is any amino acid other than Gln. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_4 is Ala. In some cases, X_1 is Ala; X_2 is Ala; X_3 is Ala; and X_4 is Ala;

[00454] APTSSSTKKT QLQLE**X_1**LLL**X_2** LQMILNGINN YKNPKLTRML T**X_3**KF**X_4**MPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFC**X_5**SIIS TLT (SEQ ID NO:196), where X_1 is any amino acid other than His; where X_2 is any amino acid other than Asp; where X_3 is any amino acid other than Phe; where X_4 is any amino acid other than Tyr; and where X_5 is any amino acid other than Gln. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_4 is Ala. In some cases, X_5 is Ala. In some cases, X_1 is Ala; X_2 is Ala; X_3 is Ala; X_4 is Ala; X_5 is Ala; and

[00455] APTSSSTKKT QLQLE**X_1**LLLD LQMILNGINN YKNPKLTRML T**X_2**KFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFC**X_3**SIIS TLT (SEQ ID NO:197), where X_1 is any amino acid other than His; where X_2 is any amino acid other than Phe; and where X_3 is any amino acid other than Gln. In some cases, X_1 is Ala. In some cases, X_2 is Ala. In some cases, X_3 is Ala. In some cases, X_1 is Ala; X_2 is Ala; and X_3 is Ala.

Additional polypeptides

[00456] A polypeptide chain of a TMMP of the present disclosure can include one or more polypeptides in addition to those described above. Suitable additional polypeptides include epitope tags and affinity domains. The one or more additional polypeptide can be included at the N-terminus of a polypeptide chain of a TMMP, at the C-terminus of a polypeptide chain of a TMMP, or internally within a polypeptide chain of a TMMP.

Epitope tag

[00457] Suitable epitope tags include, but are not limited to, hemagglutinin (HA; e.g., YPYDVPDYA (SEQ ID NO:271); FLAG (e.g., DYKDDDDK (SEQ ID NO:272); c-myc (e.g., EQKLISEEDL; SEQ ID NO:273), and the like.

Affinity domain

Affinity domains include peptide sequences that can interact with a binding partner, e.g., such as one immobilized on a solid support, useful for identification or purification. DNA sequences encoding multiple consecutive single amino acids, such as histidine, when fused to the expressed protein, may be used for one-step purification of the recombinant protein by high affinity binding to a resin column, such as nickel sepharose. Exemplary affinity domains include His5 (HHHHH) (SEQ ID NO:271), HisX6 (HHHHHH) (SEQ ID NO:275), C-myc (EQKLISEEDL) (SEQ ID NO:276), Flag (DYKDDDDK) (SEQ ID NO:277), StrepTag (WSHPQFEK) (SEQ ID NO:278), hemagglutinin, e.g., HA Tag (YPYDVPDYA) (SEQ ID NO:279), glutathione-S-transferase (GST), thioredoxin, cellulose binding domain, RYIRS (SEQ ID NO:280), Phe-His-His-Thr (SEQ ID NO:281), chitin binding domain, S-peptide, T7 peptide, SH2 domain, C-end RNA tag, WEAAAREACCRECCARA (SEQ ID NO:282), metal binding domains, e.g., zinc binding domains or calcium binding domains such as those from calcium-binding proteins, e.g., calmodulin, troponin C, calcineurin B, myosin light chain, recoverin, S-modulin, visinin, VILIP, neurocalcin, hippocalcin, frequenin, caltractin, calpain large-subunit, S100 proteins, parvalbumin, calbindin D9K, calbindin D28K, and calretinin, inteins, biotin, streptavidin, MyoD, Id, leucine zipper sequences, and maltose binding protein.**Drug conjugates**

[00458] A polypeptide chain of a TMMP of the present disclosure can comprise a small molecule drug linked (e.g., covalently attached) to the polypeptide chain. For example, where a TMMP of the present disclosure comprises an Fc polypeptide, the Fc polypeptide can comprise a covalently linked small molecule drug. In some cases, the small molecule drug is a cancer chemotherapeutic agent, e.g., a cytotoxic agent. A polypeptide chain of a TMMP of the present disclosure can comprise a cytotoxic agent linked (e.g., covalently attached) to the polypeptide chain. For example, where a TMMP of the present disclosure comprises an Fc polypeptide, the Fc polypeptide can comprise a covalently linked cytotoxic agent. Cytotoxic agents include prodrugs.

[00459] A drug (e.g., a cancer chemotherapeutic agent) can be linked directly or indirectly to a polypeptide chain of a TMMP of the present disclosure. For example, where a TMMP of the present disclosure comprises an Fc polypeptide, a drug (e.g., a cancer chemotherapeutic agent) can be linked directly or indirectly to the Fc polypeptide. Direct linkage can involve linkage directly to an amino acid side chain. Indirect linkage can be linkage via a linker. A drug (e.g., a cancer chemotherapeutic agent) can be linked to a polypeptide chain (e.g., an Fc polypeptide) of a TMMP of the present disclosure via a thioether bond, an amide bond, a carbamate bond, a disulfide bond, or an ether bond.

[00460] Linkers include cleavable linkers and non-cleavable linkers. In some cases, the linker is a protease-cleavable linker. Suitable linkers include, e.g., peptides (e.g., from 2 to 10 amino acids in length; e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids in length), alkyl chains, poly(ethylene glycol), disulfide groups, thioether groups, acid labile groups, photolabile groups, peptidase labile groups, and

esterase labile groups. Non-limiting example of suitable linkers are: i) N-succinimidyl-[(N-maleimidopropionamido)-tetraethyleneglycol]ester (NHS-PEG4-maleimide); ii) N-succinimidyl 4-(2-pyridyldithio)butanoate (SPDB); N-succinimidyl 4-(2-pyridyldithio)2-sulfobutanoate (sulfo-SPDB); N-succinimidyl 4-(2-pyridyldithio) pentanoate (SPP); N-succinimidyl-4-(N-maleimidomethyl)-cyclohexane-1-carboxy-(6-amidocaproate) (LC-SMCC); κ-maleimidoundecanoic acid N-succinimidyl ester (KMUA); γ-maleimide butyric acid N-succinimidyl ester (GMBS); ε-maleimidocaproic acid N-hydroxysuccinimide ester (EMCS); m-maleimide benzoyl-N-hydroxysuccinimide ester (MBS); N-(α-maleimidoacetoxy)-succinimide ester (AMAS); succinimidyl-6-(β-maleimidopropionamide)hexanoate (SMPH); N-succinimidyl 4-(p-maleimidophenyl)butyrate (SMPB); N-(p-maleimidophenyl)isocyanate (PMPI); N-succinimidyl 4(2-pyridylthio)pentanoate (SPP); N-succinimidyl(4-iodo-acetyl)aminobenzoate (SIAB); 6-maleimidocaproyl (MC); maleimidopropanoyl (MP); p-aminobenzyloxycarbonyl (PAB); N-succinimidyl 4-(maleimidomethyl)cyclohexanecarboxylate (SMCC); N-succinimidyl-4-(N-maleimidomethyl)-cyclohexane-1-carboxy-(6-amidocaproate), a "long chain" analog of SMCC (LC-SMCC); 3-maleimidopropanoic acid N-succinimidyl ester (BMPS); N-succinimidyl iodoacetate (SIA); N-succinimidyl bromoacetate (SBA); and N-succinimidyl 3-(bromoacetamido)propionate (SBAP).

[00461] A polypeptide (e.g., an Fc polypeptide) can be modified with crosslinking reagents such as succinimidyl 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate (SMCC), sulfo-SMCC, maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), sulfo-MBS or succinimidyl-iodoacetate, as described in the literature, to introduce 1-10 reactive groups. The modified Fc polypeptide is then reacted with a thiol-containing cytotoxic agent to produce a conjugate.

[00462] For example, where a TMMP of the present disclosure comprises an Fc polypeptide, the polypeptide chain comprising the Fc polypeptide can be of the formula (A)-(L)-(C), where (A) is the polypeptide chain comprising the Fc polypeptide; where (L), if present, is a linker; and where (C) is a cytotoxic agent. (L), if present, links (A) to (C). In some cases, the polypeptide chain comprising the Fc polypeptide can comprise more than one cytotoxic agent (e.g., 2, 3, 4, or 5, or more than 5, cytotoxic agents).

[00463] Suitable drugs include, e.g., rapamycin. Suitable drugs include, e.g., retinoids, such as all-trans retinoic acid (ATRA); vitamin D3; a vitamin D3 analog; and the like. As noted above, in some cases, a drug is a cytotoxic agent. Cytotoxic agents are known in the art. A suitable cytotoxic agent can be any compound that results in the death of a cell, or induces cell death, or in some manner decreases cell viability, and includes, for example, maytansinoids and maytansinoid analogs, benzodiazepines, taxoids, CC-1065 and CC-1065 analogs, duocarmycins and duocarmycin analogs, enediynes, such as calicheamicins, dolastatin and dolastatin analogs including auristatins, tomaymycin derivatives, leptomycin derivatives, methotrexate, cisplatin, carboplatin, daunorubicin, doxorubicin, vincristine, vinblastine, melphalan, mitomycin C, chlorambucil and morpholino doxorubicin.

[00464] For example, in some cases, the cytotoxic agent is a compound that inhibits microtubule formation in eukaryotic cells. Such agents include, e.g., maytansinoid, benzodiazepine, taxoid, CC-1065, duocarmycin, a duocarmycin analog, calicheamicin, dolastatin, a dolastatin analog, auristatin, tomaymycin, and leptomycin, or a pro-drug of any one of the foregoing. Maytansinoid compounds include, e.g., N(2')-deacetyl-N(2')-(3-mercapto-1-oxopropyl)-maytansine (DM1); N(2')-deacetyl-N(2')-(4-mercapto-1-oxopentyl)-maytansine (DM3); and N(2')-deacetyl-N2-(4-mercapto-4-methyl-1-oxopentyl)-maytansine (DM4). Benzodiazepines include, e.g., indolinobenzodiazepines and oxazolidinobenzodiazepines.

[00465] Cytotoxic agents include taxol; cytochalasin B; gramicidin D; ethidium bromide; emetine; mitomycin; etoposide; tenoposide; vincristine; vinblastine; colchicin; doxorubicin; daunorubicin; dihydroxy anthracin dione; maytansine or an analog or derivative thereof; an auristatin or a functional peptide analog or derivative thereof; dolastatin 10 or 15 or an analogue thereof; irinotecan or an analogue thereof; mitoxantrone; mithramycin; actinomycin D; 1-dehydrotestosterone; a glucocorticoid; procaine; tetracaine; lidocaine; propranolol; puromycin; calicheamicin or an analog or derivative thereof; an antimetabolite; 6 mercaptopurine; 6 thioguanine; cytarabine; fludarabin; 5 fluorouracil; decarbazine; hydroxyurea; asparaginase; gemcitabine; cladribine; an alkylating agent; a platinum derivative; duocarmycin A; duocarmycin SA; rachelmycin (CC-1065) or an analog or derivative thereof; an antibiotic; pyrrolo[2,1-c][1,4]-benzodiazepines (PDB); diphtheria toxin; ricin toxin; cholera toxin; a Shiga-like toxin; LT toxin; C3 toxin; Shiga toxin; pertussis toxin; tetanus toxin; soybean Bowman-Birk protease inhibitor; Pseudomonas exotoxin; alorin; saporin; modeccin; gelanin; abrin A chain; modeccin A chain; alpha-sarcin; *Aleurites fordii* proteins; dianthin proteins; *Phytolacca americana* proteins; momordica charantia inhibitor; curcin; crotin; sapaonaria officinalis inhibitor; gelonin; mitogellin; restrictocin; phenomycin; enomycin toxins; ribonuclease (RNase); DNase I; Staphylococcal enterotoxin A; pokeweed antiviral protein; diphtherin toxin; and Pseudomonas endotoxin.

Exemplary TMMPs

[00466] A TMMP of the present disclosure comprises at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; and ii) first MHC polypeptide; b) a second polypeptide comprising a second MHC polypeptide, and c) at least one immunomodulatory polypeptide, where the first and/or the second polypeptide comprises the immunomodulatory polypeptide. Thus, in some cases, a TMMP of the present disclosure comprises at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; ii) first MHC polypeptide; and iii) at least one immunomodulatory polypeptide; and b) a second polypeptide comprising a second MHC polypeptide. In other instances, a TMMP of the present disclosure comprises at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; and ii) first MHC polypeptide; and b) a second polypeptide comprising:

i) a second MHC polypeptide; and ii) at least one immunomodulatory polypeptide. In some cases, a TMMP of the present disclosure comprises at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope; ii) first MHC polypeptide; and iii) at least one immunomodulatory polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide; and ii) at least one immunomodulatory polypeptide. In some cases, the at least one immunomodulatory polypeptide is a wild-type immunomodulatory polypeptide. In other cases, the at least one immunomodulatory polypeptide is a variant immunomodulatory polypeptide that exhibits reduced affinity for a co-immunomodulatory polypeptide, compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the co-immunomodulatory polypeptide. In some cases, a TMMP of the present disclosure comprises two immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence. In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[00467] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a first MHC polypeptide; and iii) at least one immunomodulatory polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; and ii) an Ig Fc polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the first polypeptide comprises, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a first MHC polypeptide; and iii) two immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions. In some cases, a peptide linker is between one or more of: i) the second MHC polypeptide and the Ig Fc polypeptide; ii) the epitope and the first MHC polypeptide; iii) the first MHC polypeptide and the immunomodulatory polypeptide; and (where the TMMP comprises two immunomodulatory polypeptides on the first polypeptide chain) iv) between the two immunomodulatory polypeptides. In some cases, the peptide linker comprises the amino acid sequence AAAGG (SEQ ID NO:283). In some cases, the peptide linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO"284), where n is an integer

from 1 to 10 (e.g., where n is 2, 3, or 4). In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[00468] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) at least one immunomodulatory polypeptide; ii) a second MHC polypeptide; and iii) an Ig Fc polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the second polypeptide comprises, in order from N-terminus to C-terminus: i) two immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence; ii) a second MHC polypeptide; and iii) an Ig Fc polypeptide. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions. In some cases, a peptide linker is between one or more of: i) the second MHC polypeptide and the Ig Fc polypeptide; ii) the epitope and the first MHC polypeptide; iii) the first MHC polypeptide and the immunomodulatory polypeptide; and (where the TMMP comprises two immunomodulatory polypeptides on the second polypeptide chain) iv) between the two immunomodulatory polypeptides. In some cases, the peptide linker comprises the amino acid sequence AAAGG (SEQ ID NO: 283). In some cases, the peptide linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO: 284), where n is an integer from 1 to 10 (e.g., where n is 2, 3, or 4). In some cases, the peptide epitope present in a TMMP of the present disclosure is a cancer-associated peptide. In some cases, the peptide epitope present in a TMMP of the present disclosure is an infectious disease-associated peptide (e.g., a virus-encoded peptide).

[00469] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; ii) an Ig Fc polypeptide; and iii) at least one immunomodulatory polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the second polypeptide comprises, in order from N-terminus to C-

terminus: i) a second MHC polypeptide; ii) an Ig Fc polypeptide; and iii) two immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions. In some cases, a peptide linker is between one or more of: i) the second MHC polypeptide and the Ig Fc polypeptide; ii) the epitope and the first MHC polypeptide; iii) the Ig Fc polypeptide and the immunomodulatory polypeptide; and (where the TMMP comprises two immunomodulatory polypeptides on the second polypeptide chain) iv) between the two immunomodulatory polypeptides. In some cases, the peptide linker comprises the amino acid sequence AAAGG (SEQ ID NO:283). In some cases, the peptide linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO: 284), where n is an integer from 1 to 10 (e.g., where n is 2, 3, or 4).

[00470] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) at least one immunomodulatory polypeptide; ii) a second MHC polypeptide; and iii) an Ig Fc polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions.

[00471] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) at least one immunomodulatory polypeptide; ii) a peptide epitope; and iii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; and ii) an Ig Fc polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the first polypeptide comprises, in order from N-terminus to C-terminus: i) two

immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence; ii) a peptide epitope; and iii) a first MHC polypeptide. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions. In some cases, a peptide linker is between one or more of: i) the second MHC polypeptide and the Ig Fc polypeptide; ii) the epitope and the first MHC polypeptide; iii) the immunomodulatory polypeptide and the epitope; and (where the TMMP comprises two immunomodulatory polypeptides on the first polypeptide chain) iv) between the two immunomodulatory polypeptides. In some cases, the peptide linker comprises the amino acid sequence AAAGG (SEQ ID NO: 283). In some cases, the peptide linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO: 284), where n is an integer from 1 to 10 (e.g., where n is 2, 3, or 4).

[00472] In some cases, a TMMP of the present disclosure comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC polypeptide; ii) at least one immunomodulatory polypeptide; and iii) an Ig Fc polypeptide. In some cases, the first MHC polypeptide is a β2M polypeptide; and the second MHC polypeptide is an HLA heavy chain polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide. In some cases, the HLA heavy chain polypeptide is an HLA-A24 polypeptide with an A236C substitution. In some cases, the second polypeptide comprises, in order from N-terminus to C-terminus: i) a second MHC polypeptide; ii) two immunomodulatory polypeptides, where the two immunomodulatory polypeptides have the same amino acid sequence; and iii) an Ig Fc polypeptide. In some cases, the Ig Fc polypeptide is a human IgG1 Fc polypeptide. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide comprising L234A and L235A substitutions. In some cases, the first and the second polypeptides are disulfide linked to one another. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16A and F42A substitutions. In some cases, the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising H16T and F42A substitutions. In some cases, a peptide linker is between one or more of: i) the second MHC polypeptide and the immunomodulatory polypeptide; ii) the immunomodulatory polypeptide and the Ig Fc polypeptide; iii) the epitope and the first MHC polypeptide; iii) the first MHC polypeptide and the immunomodulatory polypeptide; and (where the TMMP comprises two immunomodulatory polypeptides on the second polypeptide chain) iv) between the two immunomodulatory polypeptides. In some cases, the peptide linker comprises the amino acid sequence AAAGG (SEQ ID NO: 283). In some cases, the peptide linker

comprises the amino acid sequence (GGGGS)n (SEQ ID NO: 284), where n is an integer from 1 to 10 (e.g., where n is 2, 3, or 4).

[00473] As noted above, and as depicted schematically in FIG. 14, an immunomodulatory polypeptide (i.e., one or more immunomodulatory polypeptides) can be present in a TMMP of the present disclosure at any of a variety of positions. FIG. 14 depicts the position of two copies of a variant IL-2 polypeptide; however, the immunomodulatory polypeptide can be any of a variety of immunomodulatory polypeptide, as described herein. As depicted in FIG. 14, an immunomodulatory polypeptide can be: 1) N-terminal to the MHC class I heavy chain (position 1); 2) C-terminal to the MHC class I heavy chain and N-terminal to the Ig Fc polypeptide; in other words, between the MHC class I heavy chain and the Ig Fc polypeptide (position 2); 3) C-terminal to the Ig Fc polypeptide (position 3); 4) N-terminal to the peptide epitope (position 4); or 5) C-terminal to the β2M polypeptide (position 5). "Position 1" refers to a position of the immunomodulatory polypeptide on the same polypeptide chain as the class I MHC heavy chain and N-terminal to the class I MHC heavy chain; e.g., where the TMMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a β2M polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more immunomodulatory polypeptides; and ii) a class I MHC heavy chain polypeptide. "Position 2" refers to a position of the immunomodulatory polypeptide on the same polypeptide chain as the class I MHC heavy chain and C-terminal to the class I MHC heavy chain, but not at the C-terminus of the polypeptide chain; e.g., where the TMMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a β2M polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a class I MHC heavy chain polypeptide; ii) one or more immunomodulatory polypeptides; and iii) an Ig Fc polypeptide. "Position 3" refers to a position of the immunomodulatory polypeptide on the same polypeptide chain as the class I MHC heavy chain and at the C-terminus of the polypeptide chain; e.g., where the TMMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; and ii) a β2M polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a class I MHC heavy chain polypeptide; ii) an Ig Fc polypeptide; and iii) one or more immunomodulatory polypeptides. "Position 4" refers to a position of the immunomodulatory polypeptide on the same polypeptide chain as the β2M polypeptide and N-terminal to the peptide epitope and the β2M polypeptide; e.g., where the TMMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) one or more immunomodulatory polypeptides; ii) a peptide epitope; and iii) a β2M polypeptide; and b) a second polypeptide comprising a class I MHC heavy chain polypeptide (e.g., a second polypeptide comprising, in order from N-terminus to C-terminus: i) a class I MHC heavy chain polypeptide; and ii) an Ig Fc polypeptide. "Position 5" refers to a position of the immunomodulatory polypeptide on the same polypeptide chain as the β2M polypeptide and C-terminal to the β2M

polypeptide (e.g., at the C-terminus of the polypeptide chain); e.g., where the TMMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a β2M polypeptide; and iii) one or more immunomodulatory polypeptides; and b) a second polypeptide comprising a class I MHC heavy chain polypeptide (e.g., a second polypeptide comprising, in order from N-terminus to C-terminus: i) a class I MHC heavy chain polypeptide; and ii) an Ig Fc polypeptide.

[00474] Furthermore, as discussed above and as depicted schematically in FIG. 13A-13C, the first polypeptide chain and the second polypeptide chain of a TMMP of the present disclosure can be linked by one or more disulfide bonds. For example, a TMMMP of the present disclosure can comprise: a) a first polypeptide chain comprising an β2M polypeptide having an R12C substitution; and b) a second polypeptide chain comprising a class I MHC heavy chain polypeptide having an A236C substitution; such that a disulfide bond forms between the Cys at position 12 of the β2M polypeptide in the first polypeptide chain and the Cys at position 236 of the class I MHC heavy chain polypeptide in the second polypeptide chain. As another example, a TMMMP of the present disclosure can comprise: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a peptide linker comprising a $GCGG(G4S)_n$ sequence, where n is 1, 2, or 3; and iii) a β2M polypeptide; and b) a second polypeptide comprising a class I MHC heavy chain polypeptide having a Y84C substitution, such that a disulfide bond forms between the Cys in the peptide linker in the first polypeptide chain and the Cys at position 84 of the class I MHC heavy chain polypeptide in the second polypeptide chain. In other examples, a TMMP of the present disclosure can comprise: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a peptide epitope; ii) a peptide linker comprising a $GCGG(G4S)_n$ sequence, where n is 1, 2, or 3; and iii) a β2M polypeptide having an R12C substitution; and b) a second polypeptide comprising a class I MHC heavy chain polypeptide having a Y84C substitution and an A236C substitution; such that: i) a first disulfide bond forms between the Cys in the peptide linker in the first polypeptide chain and the Cys at position 84 of the class I MHC heavy chain polypeptide in the second polypeptide chain; and ii) a second disulfide bond forms between the Cys at position 12 of the β2M polypeptide in the first polypeptide chain and the Cys at position 236 of the class I MHC heavy chain polypeptide in the second polypeptide chain. For simplicity, the first disulfide bond is referred to as "G2C/Y84C"; and the second disulfide bond is referred to as "R12C/A236C." A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; b) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; or c) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond.

[00475] A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; and b) at least one immunomodulatory polypeptide at position 1. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; and b) at least one immunomodulatory polypeptide at position 2. A TMMP of the present

disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; and b) at least one immunomodulatory polypeptide at position 3. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; and b) at least one immunomodulatory polypeptide at position 4. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and not an R12C/A236C disulfide bond; and b) at least one immunomodulatory polypeptide at position 5.

[00476] A TMMP of the present disclosure can include: a) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; and at least one immunomodulatory polypeptide at position 1. A TMMP of the present disclosure can include: a) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; and at least one immunomodulatory polypeptide at position 2. A TMMP of the present disclosure can include: a) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; and at least one immunomodulatory polypeptide at position 3. A TMMP of the present disclosure can include: a) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; and at least one immunomodulatory polypeptide at position 4. A TMMP of the present disclosure can include: a) an R12C/A236C disulfide bond and not a G2C/Y84C disulfide bond; and at least one immunomodulatory polypeptide at position 5.

[00477] A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond; and b) and at least one immunomodulatory polypeptide at position 1. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond; and b) and at least one immunomodulatory polypeptide at position 2. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond; and b) and at least one immunomodulatory polypeptide at position 3. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond; and b) and at least one immunomodulatory polypeptide at position 4. A TMMP of the present disclosure can include: a) a G2C/Y84C disulfide bond and an R12C/A236C disulfide bond; and b) and at least one immunomodulatory polypeptide at position 5.

METHODS OF GENERATING A MULTIMERIC T-CELL MODULATORY POLYPEPTIDE

[00478] The present disclosure provides a method of obtaining a TMMP comprising one or more variant immunomodulatory polypeptides that exhibit lower affinity for a cognate co-immunomodulatory polypeptide compared to the affinity of the corresponding parental wild-type immunomodulatory polypeptide for the co-immunomodulatory polypeptide, the method comprising: A) generating a library of TMMPs comprising a plurality of members, wherein each member comprises: a) a first polypeptide comprising: i) an epitope; and ii) a first major MHC polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide; and ii) optionally an Ig Fc polypeptide or a non-Ig scaffold, wherein each member comprises a different variant immunomodulatory polypeptide on the first

polypeptide, the second polypeptide, or both the first and the second polypeptide; B) determining the affinity of each member of the library for a cognate co-immunomodulatory polypeptide; and C) selecting a member that exhibits reduced affinity for the cognate co-immunomodulatory polypeptide. In some cases, the affinity is determined by bio-layer interferometry (BLI) using purified TMMP library members and the cognate co-immunomodulatory polypeptide. BLI methods are well known to those skilled in the art. A BLI assay is described above. See, e.g., Lad et al. (2015) J. Biomol. Screen. 20(4): 498-507; and Shah and Duncan (2014) *J. Vis. Exp.* 18:e51383.

[00479] The present disclosure provides a method of obtaining a TMMP that exhibits selective binding to a T-cell, the method comprising: A) generating a library of TMMPs comprising a plurality of members, wherein each member comprises: a) a first polypeptide comprising: i) an epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide; and ii) optionally an immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold, wherein each member comprises a different variant immunomodulatory polypeptide on the first polypeptide, the second polypeptide, or both the first and the second polypeptide, wherein the variant immunomodulatory polypeptide differs in amino acid sequence by from 1 amino acid to 10 amino acids from a parental wild-type immunomodulatory polypeptide; B) contacting a TMMP library member with a target T-cell expressing on its surface: i) a cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to the epitope, wherein the TMMP library member comprises an epitope tag, such that the TMMP library member binds to the target T-cell; C) contacting the TMMP library member bound to the target T-cell with a fluorescently labeled binding agent that binds to the epitope tag, generating a TMMP library member/target T-cell/binding agent complex; D) measuring the mean fluorescence intensity (MFI) of the TMMP library member/target T-cell/binding agent complex using flow cytometry, wherein the MFI measured over a range of concentrations of the TMMP library member provides a measure of the affinity and apparent avidity; and E) selecting a TMMP library member that selectively binds the target T cell, compared to binding of the TMMP library member to a control T cell that comprises: i) the cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to an epitope other than the epitope present in the TMMP library member. In some cases, a TMMP library member that is identified as selectively binds to a target T cell is isolated from the library.

[00480] In some cases, a parental wild-type immunomodulatory polypeptide and cognate immunomodulatory polypeptide pairs are selected from:

[00481] IL-2 and IL-2 receptor;

[00482] 4-1BBL and 4-1BB;

[00483] PD-L1 and PD-1;

[00484] CD70 and CD27;

[00485] TGFβ and TGFβ receptor;

[00486] CD80 and CD28;

[00487] CD86 and CD28;

[00488] OX40L and OX40;

[00489] FasL and Fas;

[00490] ICOS-L and ICOS;

[00491] ICAM and LFA-1;

[00492] JAG1 and Notch;

[00493] JAG1 and CD46;

[00494] CD80 and CTLA4; and

[00495] CD86 and CTLA4.

[00496] The present disclosure provides a method of obtaining a TMMP comprising one or more variant immunomodulatory polypeptides that exhibit reduced affinity for a cognate co-immunomodulatory polypeptide compared to the affinity of the corresponding parental wild-type immunomodulatory polypeptide for the co-immunomodulatory polypeptide, the method comprising selecting, from a library of TMMPs comprising a plurality of members, a member that exhibits reduced affinity for the cognate co-immunomodulatory polypeptide, wherein the plurality of member comprises: a) a first polypeptide comprising: i) an epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide; and ii) optionally an Ig Fc polypeptide or a non-Ig scaffold, wherein the members of the library comprise a plurality of variant immunomodulatory polypeptide present in the first polypeptide, the second polypeptide, or both the first and the second polypeptide. In some cases, the selecting step comprises determining the affinity, using bio-layer interferometry, of binding between TMMP library members and the cognate co-immunomodulatory polypeptide. In some cases, the TMMP is as described above.

[00497] In some cases, the method further comprises: a) contacting the selected TMMP library member with a target T-cell expressing on its surface: i) a cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to the epitope, wherein the TMMP library member comprises an epitope tag, such that the TMMP library member binds to the target T-cell; b) contacting the selected TMMP library member bound to the target T-cell with a fluorescently labeled binding agent that binds to the epitope tag, generating a selected TMMP library member/target T-cell/binding agent complex; and c) measuring the mean fluorescence intensity (MFI) of the selected TMMP library member/target T-cell/binding agent complex using flow cytometry, wherein the MFI measured over a range of concentrations of the selected TMMP library

member provides a measure of the affinity and apparent avidity. A selected TMMP library member that selectively binds the target T cell, compared to binding of the TMMP library member to a control T cell that comprises: i) the cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to an epitope other than the epitope present in the TMMP library member, is identified as selectively binding to the target T cell. In some cases, the binding agent is an antibody specific for the epitope tag. In some cases, the variant immunomodulatory polypeptide comprises from 1 to 20 amino acid substitutions (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions) compared to the corresponding parental wild-type immunomodulatory polypeptide. In some cases, the TMMP comprises two variant immunomodulatory polypeptides. In some cases, the two variant immunomodulatory polypeptides comprise the same amino acid sequence. In some cases, the first polypeptide comprises one of the two variant immunomodulatory polypeptides and wherein the second polypeptide comprises the second of the two variant immunomodulatory polypeptides. In some cases, the two variant immunomodulatory polypeptides are on the same polypeptide chain of the TMMP. In some cases, the two variant immunomodulatory polypeptides are on the first polypeptide of the TMMP. In some cases, the two variant immunomodulatory polypeptides are on the second polypeptide of the TMMP.

[00498] In some cases, the method further comprises isolating the selected TMMP library member from the library. In some cases, the method further comprises providing a nucleic acid comprising a nucleotide sequence encoding the selected TMMP library member. In some cases, the nucleic acid is present in a recombinant expression vector. In some cases, the nucleotide sequence is operably linked to a transcriptional control element that is functional in a eukaryotic cell. In some cases, the method further comprises introducing the nucleic acid into a eukaryotic host cell, and culturing the cell in a liquid medium to synthesize the encoded selected TMMP library member in the cell. In some cases, the method further comprises isolating the synthesized selected TMMP library member from the cell or from liquid culture medium comprising the cell. In some cases, the selected TMMP library member comprises an Ig Fc polypeptide. In some cases, the method further comprises conjugating a drug to the Ig Fc polypeptide. In some cases, the drug is a cytotoxic agent is selected from maytansinoid, benzodiazepine, taxoid, CC-1065, duocarmycin, a duocarmycin analog, calicheamicin, dolastatin, a dolastatin analog, auristatin, tomaymycin, and leptomycin, or a pro-drug of any one of the foregoing. In some cases, the drug is a retinoid. In some cases, the parental wild-type immunomodulatory polypeptide and the cognate immunomodulatory polypeptides are selected from: IL-2 and IL-2 receptor; 4-1BBL and 4-1BB; PD-L1 and PD-1; CD70 and CD27; TGFβ and TGFβ receptor; CD80 and CD28; CD86 and CD28; OX40L and OX40; FasL and Fas; ICOS-L and ICOS; ICAM and LFA-1; JAG1 and Notch; JAG1 and CD46; CD80 and CTLA4; and CD86 and CTLA4.

[00499] The present disclosure provides a method of obtaining a TMMP comprising one or more variant immunomodulatory polypeptides that exhibit reduced affinity for a cognate co-immunomodulatory polypeptide compared to the affinity of the corresponding parental wild-type immunomodulatory polypeptide for the co-immunomodulatory polypeptide, the method comprising: A) providing a library of TMMPs comprising a plurality of members, wherein the plurality of member comprises: a) a first polypeptide comprising: i) an epitope; and ii) a first MHC polypeptide; and b) a second polypeptide comprising: i) a second MHC polypeptide; and ii) optionally an Ig Fc polypeptide or a non-Ig scaffold, wherein the members of the library comprise a plurality of variant immunomodulatory polypeptide present in the first polypeptide, the second polypeptide, or both the first and the second polypeptide; and B) selecting from the library a member that exhibits reduced affinity for the cognate co-immunomodulatory polypeptide. In some cases, the selecting step comprises determining the affinity, using bio-layer interferometry, of binding between TMMP library members and the cognate co-immunomodulatory polypeptide. In some cases, the TMMP is as described above.

[00500] In some cases, the method further comprises: a) contacting the selected TMMP library member with a target T-cell expressing on its surface: i) a cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to the epitope, wherein the TMMP library member comprises an epitope tag, such that the TMMP library member binds to the target T-cell; b) contacting the selected TMMP library member bound to the target T-cell with a fluorescently labeled binding agent that binds to the epitope tag, generating a selected TMMP library member/target T-cell/binding agent complex; and c) measuring the mean fluorescence intensity (MFI) of the selected TMMP library member/target T-cell/binding agent complex using flow cytometry, wherein the MFI measured over a range of concentrations of the selected TMMP library member provides a measure of the affinity and apparent avidity. A selected TMMP library member that selectively binds the target T cell, compared to binding of the TMMP library member to a control T cell that comprises: i) the cognate co-immunomodulatory polypeptide that binds the parental wild-type immunomodulatory polypeptide; and ii) a T-cell receptor that binds to an epitope other than the epitope present in the TMMP library member, is identified as selectively binding to the target T cell. In some cases, the binding agent is an antibody specific for the epitope tag. In some cases, the variant immunomodulatory polypeptide comprises from 1 to 20 amino acid substitutions (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions) compared to the corresponding parental wild-type immunomodulatory polypeptide. In some cases, the TMMP comprises two variant immunomodulatory polypeptides. In some cases, the two variant immunomodulatory polypeptides comprise the same amino acid sequence. In some cases, the first polypeptide comprises one of the two variant immunomodulatory polypeptides and wherein the second polypeptide comprises the second of the two variant immunomodulatory polypeptides. In some cases, the two variant immunomodulatory

polypeptides are on the same polypeptide chain of the TMMP. In some cases, the two variant immunomodulatory polypeptides are on the first polypeptide of the TMMP. In some cases, the two variant immunomodulatory polypeptides are on the second polypeptide of the TMMP.

[00501] In some cases, the method further comprises isolating the selected TMMP library member from the library. In some cases, the method further comprises providing a nucleic acid comprising a nucleotide sequence encoding the selected TMMP library member. In some cases, the nucleic acid is present in a recombinant expression vector. In some cases, the nucleotide sequence is operably linked to a transcriptional control element that is functional in a eukaryotic cell. In some cases, the method further comprises introducing the nucleic acid into a eukaryotic host cell, and culturing the cell in a liquid medium to synthesize the encoded selected TMMP library member in the cell. In some cases, the method further comprises isolating the synthesized selected TMMP library member from the cell or from liquid culture medium comprising the cell. In some cases, the selected TMMP library member comprises an Ig Fc polypeptide. In some cases, the method further comprises conjugating a drug to the Ig Fc polypeptide. In some cases, the drug is a cytotoxic agent is selected from maytansinoid, benzodiazepine, taxoid, CC-1065, duocarmycin, a duocarmycin analog, calicheamicin, dolastatin, a dolastatin analog, auristatin, tomaymycin, and leptomycin, or a pro-drug of any one of the foregoing. In some cases, the drug is a retinoid. In some cases, the parental wild-type immunomodulatory polypeptide and the cognate immunomodulatory polypeptides are selected from IL-2 and IL-2 receptor; 4-1BBL and 4-1BB; PD-L1 and PD-1; TGFβ and TGFβ receptor; CD80 and CD28; CD86 and CD28; OX40L and OX40; FasL and Fas; ICOS-L and ICOS; CD70 and CD27; ICAM and LFA-1; JAG1 and Notch; JAG1 and CD46; CD80 and CTLA4; and CD86 and CTLA4.

NUCLEIC ACIDS

[00502] The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a TMMP of the present disclosure. The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a TMMP of the present disclosure.

[00503] The present disclosure provides nucleic acids comprising nucleotide sequences encoding a TMMP of the present disclosure. In some cases, the individual polypeptide chains of a TMMP of the present disclosure are encoded in separate nucleic acids. In some cases, all polypeptide chains of a TMMP of the present disclosure are encoded in a single nucleic acid. In some cases, a first nucleic acid comprises a nucleotide sequence encoding a first polypeptide of a TMMP of the present disclosure; and a second nucleic acid comprises a nucleotide sequence encoding a second polypeptide of a TMMP of the present disclosure. In some cases, single nucleic acid comprises a nucleotide sequence encoding a first polypeptide of a TMMP of the present disclosure and a second polypeptide of a TMMP of the present disclosure.

Separate nucleic acids encoding individual polypeptide chains of a multimeric polypeptide

[00504] The present disclosure provides nucleic acids comprising nucleotide sequences encoding a TMMP of the present disclosure. As noted above, in some cases, the individual polypeptide chains of a TMMP of the present disclosure are encoded in separate nucleic acids. In some cases, nucleotide sequences encoding the separate polypeptide chains of a TMMP of the present disclosure are operably linked to transcriptional control elements, e.g., promoters, such as promoters that are functional in a eukaryotic cell, where the promoter can be a constitutive promoter or an inducible promoter.

[00505] The present disclosure provides a first nucleic acid and a second nucleic acid, where the first nucleic acid comprises a nucleotide sequence encoding a first polypeptide of a TMMP of the present disclosure, where the first polypeptide comprises, in order from N-terminus to C-terminus: a) an epitope (e.g., a T-cell epitope); b) a first MHC polypeptide; and c) an immunomodulatory polypeptide (e.g., a reduced-affinity variant, as described above); and where the second nucleic acid comprises a nucleotide sequence encoding a second polypeptide of a TMMP of the present disclosure, where the second polypeptide comprises, in order from N-terminus to C-terminus: a) a second MHC polypeptide; and b) an Ig Fc polypeptide. Suitable T-cell epitopes, MHC polypeptides, immunomodulatory polypeptides, and Ig Fc polypeptides, are described above. In some cases, the nucleotide sequences encoding the first and the second polypeptides are operably linked to transcriptional control elements. In some cases, the transcriptional control element is a promoter that is functional in a eukaryotic cell. In some cases, the nucleic acids are present in separate expression vectors.

[00506] The present disclosure provides a first nucleic acid and a second nucleic acid, where the first nucleic acid comprises a nucleotide sequence encoding a first polypeptide of a TMMP of the present disclosure, where the first polypeptide comprises, in order from N-terminus to C-terminus: a) an epitope (e.g., a T-cell epitope); and b) a first MHC polypeptide; and where the second nucleic acid comprises a nucleotide sequence encoding a second polypeptide of a TMMP of the present disclosure, where the second polypeptide comprises, in order from N-terminus to C-terminus: a) an immunomodulatory polypeptide (e.g., a reduced-affinity variant as described above); b) a second MHC polypeptide; and c) an Ig Fc polypeptide. Suitable T-cell epitopes, MHC polypeptides, immunomodulatory polypeptides, and Ig Fc polypeptides, are described above. In some cases, the nucleotide sequences encoding the first and the second polypeptides are operably linked to transcriptional control elements. In some cases, the transcriptional control element is a promoter that is functional in a eukaryotic cell. In some cases, the nucleic acids are present in separate expression vectors.

Nucleic acid encoding two or more polypeptides present in a multimeric polypeptide

[00507] The present disclosure provides a nucleic acid comprising nucleotide sequences encoding at least the first polypeptide and the second polypeptide of a TMMP of the present disclosure. In some cases, where a TMMP of the present disclosure includes a first, second, and third polypeptide, the

nucleic acid includes a nucleotide sequence encoding the first, second, and third polypeptides. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMMP of the present disclosure includes a proteolytically cleavable linker interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMMP of the present disclosure includes an internal ribosome entry site (IRES) interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMMP of the present disclosure includes a ribosome skipping signal (or *cis*-acting hydrolase element, CHYSEL) interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. Examples of nucleic acids are described below, where a proteolytically cleavable linker is provided between nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMMP of the present disclosure; in any of these embodiments, an IRES or a ribosome skipping signal can be used in place of the nucleotide sequence encoding the proteolytically cleavable linker.

[00508] In some cases, a first nucleic acid (e.g., a recombinant expression vector, an mRNA, a viral RNA, etc.) comprises a nucleotide sequence encoding a first polypeptide chain of a TMMP of the present disclosure; and a second nucleic acid (e.g., a recombinant expression vector, an mRNA, a viral RNA, etc.) comprises a nucleotide sequence encoding a second polypeptide chain of a TMMP of the present disclosure. In some cases, the nucleotide sequence encoding the first polypeptide, and the second nucleotide sequence encoding the second polypeptide, are each operably linked to transcriptional control elements, e.g., promoters, such as promoters that are functional in a eukaryotic cell, where the promoter can be a constitutive promoter or an inducible promoter.

[00509] The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a recombinant polypeptide, where the recombinant polypeptide comprises, in order from N-terminus to C-terminus: a) an epitope (e.g., a T-cell epitope); b) a first MHC polypeptide; c) an immunomodulatory polypeptide (e.g., a reduced-affinity variant as described above); d) a proteolytically cleavable linker; e) a second MHC polypeptide; and f) an immunoglobulin (Ig) Fc polypeptide. The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a recombinant polypeptide, where the recombinant polypeptide comprises, in order from N-terminus to C-terminus: a) a first leader peptide; b) the epitope; c) the first MHC polypeptide; d) the immunomodulatory polypeptide (e.g., a reduced-affinity variant as described above); e) the proteolytically cleavable linker; f) a second leader peptide; g) the second MHC polypeptide; and h) the Ig Fc polypeptide. The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a recombinant polypeptide, where the recombinant polypeptide comprises, in order from N-terminus to C-terminus: a) an epitope; b) a first

MHC polypeptide; c) a proteolytically cleavable linker; d) an immunomodulatory polypeptide (e.g., a reduced-affinity variant as described above); e) a second MHC polypeptide; and f) an Ig Fc polypeptide. In some cases, the first leader peptide and the second leader peptide are a β2-M leader peptide. In some cases, the nucleotide sequence is operably linked to a transcriptional control element. In some cases, the transcriptional control element is a promoter that is functional in a eukaryotic cell.

[00510] Suitable MHC polypeptides are described above. In some cases, the first MHC polypeptide is a β2-microglobulin polypeptide; and wherein the second MHC polypeptide is an MHC class I heavy chain polypeptide. In some cases, the β2-microglobulin polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to a β2M amino acid sequence depicted in FIG. 4. In some cases, the MHC class I heavy chain polypeptide is an HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, HLA-G, HLA-K, or HLA-L heavy chain.

[00511] Suitable Fc polypeptides are described above. In some cases, the Ig Fc polypeptide is an IgG1 Fc polypeptide, an IgG2 Fc polypeptide, an IgG3 Fc polypeptide, an IgG4 Fc polypeptide, an IgA Fc polypeptide, or an IgM Fc polypeptide. In some cases, the Ig Fc polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to an amino acid sequence depicted in FIGs. 3A-3G.

[00512] Suitable immunomodulatory polypeptides are described above.

[00513] Suitable proteolytically cleavable linkers are described above. In some cases, the proteolytically cleavable linker comprises an amino acid sequence selected from: a) LEVLFQGP (SEQ ID NO:388); b) ENLYTQS (SEQ ID NO:389); c) DDDDK (SEQ ID NO:390); d) LVPR (SEQ ID NO:391); and e) GSGATNFSLLKQAGDVEENPGP (SEQ ID NO:392).

[00514] In some cases, a linker between the epitope and the first MHC polypeptide comprises a first Cys residue, and the second MHC polypeptide comprises an amino acid substitution to provide a second Cys residue, such that the first and the second Cys residues provide for a disulfide linkage between the linker and the second MHC polypeptide. In some cases, first MHC polypeptide comprises an amino acid substitution to provide a first Cys residue, and the second MHC polypeptide comprises an amino acid substitution to provide a second Cys residue, such that the first Cys residue and the second Cys residue provide for a disulfide linkage between the first MHC polypeptide and the second MHC polypeptide.

Recombinant expression vectors

[00515] The present disclosure provides recombinant expression vectors comprising nucleic acids of the present disclosure. In some cases, the recombinant expression vector is a non-viral vector. In some cases, the recombinant expression vector is a viral construct, e.g., a recombinant adeno-associated virus

construct (see, e.g., U.S. Patent No. 7,078,387), a recombinant adenoviral construct, a recombinant lentiviral construct, a recombinant retroviral construct, a non-integrating viral vector, etc.

[00516] Suitable expression vectors include, but are not limited to, viral vectors (e.g. viral vectors based on vaccinia virus; poliovirus; adenovirus (see, e.g., Li et al., Invest Opthalmol Vis Sci 35:2543 2549, 1994; Borras et al., Gene Ther 6:515 524, 1999; Li and Davidson, PNAS 92:7700 7704, 1995; Sakamoto et al., H Gene Ther 5:1088 1097, 1999; WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655); adeno-associated virus (see, e.g., Ali et al., Hum Gene Ther 9:81 86, 1998, Flannery et al., PNAS 94:6916 6921, 1997; Bennett et al., Invest Opthalmol Vis Sci 38:2857 2863, 1997; Jomary et al., Gene Ther 4:683 690, 1997, Rolling et al., Hum Gene Ther 10:641 648, 1999; Ali et al., Hum Mol Genet 5:591 594, 1996; Srivastava in WO 93/09239, Samulski et al., J. Vir. (1989) 63:3822-3828; Mendelson et al., Virol. (1988) 166:154-165; and Flotte et al., PNAS (1993) 90:10613-10617); SV40; herpes simplex virus; human immunodeficiency virus (see, e.g., Miyoshi et al., PNAS 94:10319 23, 1997; Takahashi et al., J Virol 73:7812 7816, 1999); a retroviral vector (e.g., Murine Leukemia Virus, spleen necrosis virus, and vectors derived from retroviruses such as Rous Sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, a lentivirus, human immunodeficiency virus, myeloproliferative sarcoma virus, and mammary tumor virus); and the like.

[00517] Numerous suitable expression vectors are known to those of skill in the art, and many are commercially available. The following vectors are provided by way of example; for eukaryotic host cells: pXT1, pSG5 (Stratagene), pSVK3, pBPV, pMSG, and pSVLSV40 (Pharmacia). However, any other vector may be used so long as it is compatible with the host cell.

[00518] Depending on the host/vector system utilized, any of a number of suitable transcription and translation control elements, including constitutive and inducible promoters, transcription enhancer elements, transcription terminators, etc. may be used in the expression vector (see e.g., Bitter et al. (1987) *Methods in Enzymology*, 153:516-544).

[00519] In some cases, a nucleotide sequence encoding a DNA-targeting RNA and/or a site-directed modifying polypeptide is operably linked to a control element, e.g., a transcriptional control element, such as a promoter. The transcriptional control element may be functional in either a eukaryotic cell, e.g., a mammalian cell; or a prokaryotic cell (e.g., bacterial or archaeal cell). In some cases, a nucleotide sequence encoding a DNA-targeting RNA and/or a site-directed modifying polypeptide is operably linked to multiple control elements that allow expression of the nucleotide sequence encoding a DNA-targeting RNA and/or a site-directed modifying polypeptide in both prokaryotic and eukaryotic cells.

[00520] Non-limiting examples of suitable eukaryotic promoters (promoters functional in a eukaryotic cell) include those from cytomegalovirus (CMV) immediate early, herpes simplex virus

(HSV) thymidine kinase, early and late SV40, long terminal repeats (LTRs) from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. The expression vector may also contain a ribosome binding site for translation initiation and a transcription terminator. The expression vector may also include appropriate sequences for amplifying expression.

GENETICALLY MODIFIED HOST CELLS

[00521] The present disclosure provides a genetically modified host cell, where the host cell is genetically modified with a nucleic acid of the present disclosure.

[00522] Suitable host cells include eukaryotic cells, such as yeast cells, insect cells, and mammalian cells. In some cases, the host cell is a cell of a mammalian cell line. Suitable mammalian cell lines include human cell lines, non-human primate cell lines, rodent (e.g., mouse, rat) cell lines, and the like. Suitable mammalian cell lines include, but are not limited to, HeLa cells (e.g., American Type Culture Collection (ATCC) No. CCL-2), CHO cells (e.g., ATCC Nos. CRL9618, CCL61, CRL9096), 293 cells (e.g., ATCC No. CRL-1573), Vero cells, NIH 3T3 cells (e.g., ATCC No. CRL-1658), Huh-7 cells, BHK cells (e.g., ATCC No. CCL10), PC12 cells (ATCC No. CRL1721), COS cells, COS-7 cells (ATCC No. CRL1651), RAT1 cells, mouse L cells (ATCC No. CCLI.3), human embryonic kidney (HEK) cells (ATCC No. CRL1573), HLHepG2 cells, and the like.

[00523] In some cases, the host cell is a mammalian cell that has been genetically modified such that it does not synthesize endogenous MHC β2-M.

[00524] In some cases, the host cell is a mammalian cell that has been genetically modified such that it does not synthesize endogenous MHC Class I heavy chain. In some cases, the host cell is a mammalian cell that has been genetically modified such that it does not synthesize endogenous MHC β2-M and such that it does not synthesize endogenous MHC Class I heavy chain.

COMPOSITIONS

[00525] The present disclosure provides compositions, including pharmaceutical compositions, comprising a TMMP (synTac) of the present disclosure. The present disclosure provides compositions, including pharmaceutical compositions, comprising a TMMP of the present disclosure. The present disclosure provides compositions, including pharmaceutical compositions, comprising a nucleic acid or a recombinant expression vector of the present disclosure.

Compositions comprising a multimeric polypeptide

[00526] A composition of the present disclosure can comprise, in addition to a TMMP of the present disclosure, one or more of: a salt, e.g., NaCl, $MgCl_2$, KCl, $MgSO_4$, etc.; a buffering agent, e.g., a Tris buffer, N-(2-Hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES), 2-(N-Morpholino)ethanesulfonic acid (MES), 2-(N-Morpholino)ethanesulfonic acid sodium salt (MES), 3-(N-

Morpholino)propanesulfonic acid (MOPS), N-tris[Hydroxymethyl]methyl-3-aminopropanesulfonic acid (TAPS), etc.; a solubilizing agent; a detergent, e.g., a non-ionic detergent such as Tween-20, etc.; a protease inhibitor; glycerol; and the like.

[00527] The composition may comprise a pharmaceutically acceptable excipient, a variety of which are known in the art and need not be discussed in detail herein. Pharmaceutically acceptable excipients have been amply described in a variety of publications, including, for example, "Remington: The Science and Practice of Pharmacy", 19th Ed. (1995), or latest edition, Mack Publishing Co; A. Gennaro (2000) "Remington: The Science and Practice of Pharmacy", 20th edition, Lippincott, Williams, & Wilkins; Pharmaceutical Dosage Forms and Drug Delivery Systems (1999) H.C. Ansel et al., eds 7th ed., Lippincott, Williams, & Wilkins; and Handbook of Pharmaceutical Excipients (2000) A.H. Kibbe et al., eds., 3rd ed. Amer. Pharmaceutical Assoc.

[00528] A pharmaceutical composition can comprise a TMMP of the present disclosure, and a pharmaceutically acceptable excipient. In some cases, a subject pharmaceutical composition will be suitable for administration to a subject, e.g., will be sterile. For example, in some cases, a subject pharmaceutical composition will be suitable for administration to a human subject, e.g., where the composition is sterile and is free of detectable pyrogens and/or other toxins.

[00529] The protein compositions may comprise other components, such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharin, talcum, cellulose, glucose, sucrose, magnesium, carbonate, and the like. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, for example, sodium acetate, sodium chloride, potassium chloride, calcium chloride, sodium lactate, hydrochloride, sulfate salts, solvates (e.g., mixed ionic salts, water, organics), hydrates (e.g., water), and the like.

[00530] For example, compositions may include aqueous solution, powder form, granules, tablets, pills, suppositories, capsules, suspensions, sprays, and the like. The composition may be formulated according to the various routes of administration described below.

[00531] Where a TMMP of the present disclosure is administered as an injectable (e.g. subcutaneously, intraperitoneally, intramuscularly, and/or intravenously) directly into a tissue, a formulation can be provided as a ready-to-use dosage form, or as non-aqueous form (e.g. a reconstitutable storage-stable powder) or aqueous form, such as liquid composed of pharmaceutically acceptable carriers and excipients. The protein-containing formulations may also be provided so as to enhance serum half-life of the TMMP following administration. For example, the TMMP may be provided in a liposome formulation, prepared as a colloid, or other conventional techniques for extending serum half-life. A variety of methods are available for preparing liposomes, as described in, e.g., Szoka

et al. 1980 *Ann. Rev. Biophys. Bioeng.* 9:467, U.S. Pat. Nos. 4,235,871, 4,501,728 and 4,837,028. The preparations may also be provided in controlled release or slow-release forms.

[00532] Other examples of formulations suitable for parenteral administration include isotonic sterile injection solutions, anti-oxidants, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. For example, a subject pharmaceutical composition can be present in a container, e.g., a sterile container, such as a syringe. The formulations can be presented in unit-dose or multi-dose sealed containers, such as ampules and vials, and can be stored in a freeze-dried (lyophilized) condition requiring only the addition of the sterile liquid excipient, for example, water, for injections, immediately prior to use. Extemporaneous injection solutions and suspensions can be prepared from sterile powders, granules, and tablets.

[00533] The concentration of a TMMP of the present disclosure in a formulation can vary widely (e.g., from less than about 0.1%, usually at or at least about 2% to as much as 20% to 50% or more by weight) and will usually be selected primarily based on fluid volumes, viscosities, and patient-based factors in accordance with the particular mode of administration selected and the patient's needs.

[00534] The present disclosure provides a container comprising a composition of the present disclosure, e.g., a liquid composition. The container can be, e.g., a syringe, an ampoule, and the like. In some cases, the container is sterile. In some cases, both the container and the composition are sterile.

[00535] The present disclosure provides compositions, including pharmaceutical compositions, comprising a TMMP of the present disclosure. A composition can comprise: a) a TMMP of the present disclosure; and b) an excipient, as described above. In some cases, the excipient is a pharmaceutically acceptable excipient.

[00536] In some cases, a TMMP of the present disclosure is present in a liquid composition. Thus, the present disclosure provides compositions (e.g., liquid compositions, including pharmaceutical compositions) comprising a TMMP of the present disclosure. In some cases, a composition of the present disclosure comprises: a) a TMMP of the present disclosure; and b) saline (e.g., 0.9% NaCl). In some cases, the composition is sterile. In some cases, the composition is suitable for administration to a human subject, e.g., where the composition is sterile and is free of detectable pyrogens and/or other toxins. Thus, the present disclosure provides a composition comprising: a) a TMMP of the present disclosure; and b) saline (e.g., 0.9% NaCl), where the composition is sterile and is free of detectable pyrogens and/or other toxins.

Compositions comprising a nucleic acid or a recombinant expression vector

[00537] The present disclosure provides compositions, e.g., pharmaceutical compositions, comprising a nucleic acid or a recombinant expression vector of the present disclosure. A wide variety of

pharmaceutically acceptable excipients is known in the art and need not be discussed in detail herein. Pharmaceutically acceptable excipients have been amply described in a variety of publications, including, for example, A. Gennaro (2000) "Remington: The Science and Practice of Pharmacy", 20th edition, Lippincott, Williams, & Wilkins; Pharmaceutical Dosage Forms and Drug Delivery Systems (1999) H. C. Ansel et al., eds 7th ed., Lippincott, Williams, & Wilkins; and Handbook of Pharmaceutical Excipients (2000) A. H. Kibbe et al., eds., 3rd ed. Amer. Pharmaceutical Assoc.

[00538] A composition of the present disclosure can include: a) one or more nucleic acids or one or more recombinant expression vectors comprising nucleotide sequences encoding a TMMP; and b) one or more of: a buffer, a surfactant, an antioxidant, a hydrophilic polymer, a dextrin, a chelating agent, a suspending agent, a solubilizer, a thickening agent, a stabilizer, a bacteriostatic agent, a wetting agent, and a preservative. Suitable buffers include, but are not limited to, (such as N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES), bis(2-hydroxyethyl)amino-tris(hydroxymethyl)methane (BIS-Tris), N-(2-hydroxyethyl)piperazine-N'3-propanesulfonic acid (EPPS or HEPPS), glycylglycine, N-2-hydroxyehtylpiperazine-N'-2-ethanesulfonic acid (HEPES), 3-(N-morpholino)propane sulfonic acid (MOPS), piperazine-N,N'-bis(2-ethane-sulfonic acid) (PIPES), sodium bicarbonate, 3-(N-tris(hydroxymethyl)-methyl-amino)-2-hydroxy-propanesulfonic acid) TAPSO, (N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid (TES), N-tris(hydroxymethyl)methyl-glycine (Tricine), tris(hydroxymethyl)-aminomethane (Tris), etc.). Suitable salts include, e.g., NaCl, $MgCl_2$, KCl, $MgSO_4$, etc.

[00539] A pharmaceutical formulation of the present disclosure can include a nucleic acid or recombinant expression vector of the present disclosure in an amount of from about 0.001% to about 90% (w/w). In the description of formulations, below, "subject nucleic acid or recombinant expression vector" will be understood to include a nucleic acid or recombinant expression vector of the present disclosure. For example, in some cases, a subject formulation comprises a nucleic acid or recombinant expression vector of the present disclosure.

[00540] A subject nucleic acid or recombinant expression vector can be admixed, encapsulated, conjugated or otherwise associated with other compounds or mixtures of compounds; such compounds can include, e.g., liposomes or receptor-targeted molecules. A subject nucleic acid or recombinant expression vector can be combined in a formulation with one or more components that assist in uptake, distribution and/or absorption.

[00541] A subject nucleic acid or recombinant expression vector composition can be formulated into any of many possible dosage forms such as, but not limited to, tablets, capsules, gel capsules, liquid syrups, soft gels, suppositories, and enemas. A subject nucleic acid or recombinant expression vector composition can also be formulated as suspensions in aqueous, non-aqueous or mixed media. Aqueous suspensions may further contain substances which increase the viscosity of the suspension including, for

example, sodium carboxymethylcellulose, sorbitol and/or dextran. The suspension may also contain stabilizers.

[00542] A formulation comprising a subject nucleic acid or recombinant expression vector can be a liposomal formulation. As used herein, the term "liposome" means a vesicle composed of amphiphilic lipids arranged in a spherical bilayer or bilayers. Liposomes are unilamellar or multilamellar vesicles which have a membrane formed from a lipophilic material and an aqueous interior that contains the composition to be delivered. Cationic liposomes are positively charged liposomes that can interact with negatively charged DNA molecules to form a stable complex. Liposomes that are pH sensitive or negatively charged are believed to entrap DNA rather than complex with it. Both cationic and noncationic liposomes can be used to deliver a subject nucleic acid or recombinant expression vector.

[00543] Liposomes also include "sterically stabilized" liposomes, a term which, as used herein, refers to liposomes comprising one or more specialized lipids that, when incorporated into liposomes, result in enhanced circulation lifetimes relative to liposomes lacking such specialized lipids. Examples of sterically stabilized liposomes are those in which part of the vesicle-forming lipid portion of the liposome comprises one or more glycolipids or is derivatized with one or more hydrophilic polymers, such as a polyethylene glycol (PEG) moiety. Liposomes and their uses are further described in U.S. Pat. No. 6,287,860, which is incorporated herein by reference in its entirety.

[00544] The formulations and compositions of the present disclosure may also include surfactants. The use of surfactants in drug products, formulations and in emulsions is well known in the art. Surfactants and their uses are further described in U.S. Pat. No. 6,287,860.

[00545] In one embodiment, various penetration enhancers are included, to effect the efficient delivery of nucleic acids. In addition to aiding the diffusion of non-lipophilic drugs across cell membranes, penetration enhancers also enhance the permeability of lipophilic drugs. Penetration enhancers may be classified as belonging to one of five broad categories, i.e., surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactants. Penetration enhancers and their uses are further described in U.S. Pat. No. 6,287,860, which is incorporated herein by reference in its entirety.

[00546] Compositions and formulations for oral administration include powders or granules, microparticulates, nanoparticulates, suspensions or solutions in water or non-aqueous media, capsules, gel capsules, sachets, tablets, or minitablets. Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids or binders may be desirable. Suitable oral formulations include those in which a subject antisense nucleic acid is administered in conjunction with one or more penetration enhancers surfactants and chelators. Suitable surfactants include, but are not limited to, fatty acids and/or esters or salts thereof, bile acids and/or salts thereof. Suitable bile acids/salts and fatty acids and their uses are further described in U.S. Pat. No. 6,287,860. Also suitable are combinations of penetration enhancers, for example, fatty

acids/salts in combination with bile acids/salts. An exemplary suitable combination is the sodium salt of lauric acid, capric acid, and UDCA. Further penetration enhancers include, but are not limited to, polyoxyethylene-9-lauryl ether, and polyoxyethylene-20-cetyl ether. Suitable penetration enhancers also include propylene glycol, dimethylsulfoxide, triethanoiamine, N,N-dimethylacetamide, N,N-dimethylformamide, 2-pyrrolidone and derivatives thereof, tetrahydrofurfuryl alcohol, and AZONE™.

METHODS OF MODULATING T CELL ACTIVITY

[00547] The present disclosure provides a method of selectively modulating the activity of an epitope-specific T cell, the method comprising contacting the T cell with a TMMP of the present disclosure, where contacting the T cell with a TMMP of the present disclosure selectively modulates the activity of the epitope-specific T cell. In some cases, the contacting occurs *in vitro*. In some cases, the contacting occurs *in vivo*. In some cases, the contacting occurs *ex vivo*.

[00548] In some cases, e.g., where the target T cell is a $CD8^+$ T cell, the TMMP comprises Class I MHC polypeptides (e.g., β2-microglobulin and Class I MHC heavy chain).

[00549] Where a TMMP of the present disclosure includes an immunomodulatory polypeptide that is an activating polypeptide, contacting the T cell with the TMMP activates the epitope-specific T cell. In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a cancer cell, and contacting the epitope-specific T cell with the TMMP increases cytotoxic activity of the T cell toward the cancer cell. In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a cancer cell, and contacting the epitope-specific T cell with the TMMP increases the number of the epitope-specific T cells.

[00550] In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a virus-infected cell, and contacting the epitope-specific T cell with the TMMP increases cytotoxic activity of the T cell toward the virus-infected cell. In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a virus-infected cell, and contacting the epitope-specific T cell with the TMMP increases the number of the epitope-specific T cells.

[00551] Where a TMMP of the present disclosure includes an immunomodulatory polypeptide that is an inhibiting polypeptide, contacting the T cell with the TMMP inhibits the epitope-specific T cell. In some instances, the epitope-specific T cell is a self-reactive T cell that is specific for an epitope present in a self antigen, and the contacting reduces the number of the self-reactive T cells.

[00552] The present disclosure provides a method of modulating an immune response in an individual, the method comprising administering to the individual an effective amount of a TMMP of the present disclosure. Administering the TMMP induces an epitope-specific T cell response (e.g., cancer epitope-specific T-cell response; a virus epitope-specific) and an epitope-non-specific T cell response, where the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at

least 2:1. In some cases, the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 5:1. In some cases, the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 10:1. In some cases, the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 25:1. In some cases, the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 50:1. In some cases, the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 100:1. In some cases, the individual is a human. In some cases, the modulating increases a cytotoxic T-cell response to a cancer cell, e.g., a cancer cell expressing an antigen that displays the same epitope displayed by the peptide epitope present in the TMMP. In some cases, the administering is intravenous, subcutaneous, intramuscular, systemic, intralymphatic, distal to a treatment site, local, or at or near a treatment site.

[00553] The present disclosure provides a method of delivering a costimulatory (i.e., immunomodulatory) polypeptide selectively to target T cell, the method comprising contacting a mixed population of T cells with a TMMP of the present disclosure, where the mixed population of T cells comprises the target T cell and non-target T cells, where the target T cell is specific for the epitope present within the TMMP (e.g., where the target T cell is specific for the epitope present within the TMMP), and where the contacting step delivers the one or more costimulatory polypeptides (immunomodulatory polypeptides) present within the TMMP to the target T cell. In some cases, the population of T cells is *in vitro*. In some cases, the population of T cells is *in vivo* in an individual. In some cases, the method comprises administering the TMMP to the individual. In some case, the T cell is a cytotoxic T cell. In some cases, the mixed population of T cells is an *in vitro* population of mixed T cells obtained from an individual, and the contacting step results in activation and/or proliferation of the target T cell, generating a population of activated and/or proliferated target T cells; in some of these instances, the method further comprises administering the population of activated and/or proliferated target T cells to the individual.

[00554] The present disclosure provides a method of detecting, in a mixed population of T cells obtained from an individual, the presence of a target T cell that binds an epitope of interest (e.g., a cancer epitope, a virus epitope), the method comprising: a) contacting *in vitro* the mixed population of T cells with a TMMP of the present disclosure, wherein the TMMP comprises the epitope of interest (e.g., the cancer epitope, the virus epitope); and b) detecting activation and/or proliferation of T cells in response to said contacting, wherein activated and/or proliferated T cells indicates the presence of the target T cell.

TREATMENT METHODS

[00555] The present disclosure provides a method of treatment of an individual, the method comprising administering to the individual an amount of a TMMP of the present disclosure, or one or more nucleic acids encoding the TMMP, effective to treat the individual. Also provided is a TMMP of

the present disclosure for use in a method of treatment of the human or animal body. In some cases, a treatment method of the present disclosure comprises administering to an individual in need thereof one or more recombinant expression vectors comprising nucleotide sequences encoding a TMMP of the present disclosure. In some cases, a treatment method of the present disclosure comprises administering to an individual in need thereof one or more mRNA molecules comprising nucleotide sequences encoding a TMMP of the present disclosure. In some cases, a treatment method of the present disclosure comprises administering to an individual in need thereof a TMMP of the present disclosure. Conditions that can be treated include, e.g., cancer and autoimmune disorders, as described below.

[00556] In some cases, a TMMP of the present disclosure, when administered to an individual in need thereof, induces both an epitope-specific T cell response and an epitope non-specific T cell response. In other words, in some cases, a TMMP of the present disclosure, when administered to an individual in need thereof, induces an epitope-specific T cell response by modulating the activity of a first T cell that displays both: i) a TCR specific for the epitope present in the TMMP; ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP; and induces an epitope non-specific T cell response by modulating the activity of a second T cell that displays: i) a TCR specific for an epitope other than the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP. The ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 2:1, at least 5:1, at least 10:1, at least 15:1, at least 20:1, at least 25:1, at least 50:1, or at least 100:1. The ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is from about 2:1 to about 5:1, from about 5:1 to about 10:1, from about 10:1 to about 15:1, from about 15:1 to about 20:1, from about 20:1 to about 25:1, from about 25:1 to about 50:1, or from about 50:1 to about 100:1, or more than 100:1. "Modulating the activity" of a T cell can include one or more of: i) activating a cytotoxic (e.g., $CD8^+$) T cell; ii) inducing cytotoxic activity of a cytotoxic (e.g., $CD8^+$) T cell; iii) inducing production and release of a cytotoxin (e.g., a perforin; a granzyme; a granulysin) by a cytotoxic (e.g., $CD8^+$) T cell; iv) inhibiting activity of an autoreactive T cell; and the like.

[00557] The combination of the reduced affinity of the immunomodulatory polypeptide for its cognate co-immunomodulatory polypeptide, and the affinity of the epitope for a TCR, provides for enhanced selectivity of a TMMP of the present disclosure. Thus, for example, a TMMP of the present disclosure binds with higher avidity to a first T cell that displays both: i) a TCR specific for the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP, compared to the avidity to which it binds to a second T cell that displays: i) a TCR specific for an epitope other than the epitope present in the TMMP; and ii) a co-immunomodulatory polypeptide that binds to the immunomodulatory polypeptide present in the TMMP.

[00558] The present disclosure provides a method of selectively modulating the activity of an epitope-specific T cell in an individual, the method comprising administering to the individual an effective amount of a TMMP of the present disclosure, or one or more nucleic acids (e.g., expression vectors; mRNA; etc.) comprising nucleotide sequences encoding the TMMP, where the TMMP selectively modulates the activity of the epitope-specific T cell in the individual. Selectively modulating the activity of an epitope-specific T cell can treat a disease or disorder in the individual. Thus, the present disclosure provides a treatment method comprising administering to an individual in need thereof an effective amount of a TMMP of the present disclosure.

[00559] In some cases, the immunomodulatory polypeptide ("MOD") is an activating polypeptide, and the TMMP activates the epitope-specific T cell. In some cases, the epitope is a cancer-associated epitope, and the TMMP increases the activity of a T cell specific for the cancer-associate epitope. In some cases, the MOD is an activating polypeptide, and the TMMP activates an epitope-specific T-cell. In some cases, the T cells are T-helper cells ($CD4^+$ cells), cytotoxic T-cells ($CD8^+$ cells), or NK-T-cells. In some cases, the epitope is a cancer epitope, and the TMMP increases the activity of a T-cell specific for a cancer cell expressing the cancer epitope (e.g., T-helper cells ($CD4^+$ cells), cytotoxic T-cells ($CD8^+$ cells), and/or NK-T-cells). Activation of $CD4^+$ T cells can include increasing proliferation of $CD4^+$ T cells and/or inducing or enhancing release cytokines by $CD4^+$ T cells. Activation of NK-T-cells and/or CD8+ cells can include: increasing proliferation of NK-T-cells and/or CD8+ cells; and/or inducing release of cytokines such as interferon γ by NK-T-cells and/or CD8+ cells. In some cases, a TMMP of the present disclosure reduces proliferation and/or activity of a regulatory T (Treg) cell. Tregs are $FoxP3^+$, $CD4^+$ T cells. In some cases, e.g., where a TMMP of the present disclosure comprises an inhibitory immunomodulatory polypeptide (e.g., PD-L1, FasL, and the like), the TMMP reduces the proliferation and/or activity of a Treg.

[00560] Where a TMMP of the present disclosure comprises a cancer peptide epitope, the TMMP can be administered to an individual in need thereof to treat a cancer in the individual, where the cancer expresses the cancer peptide epitope present in the TMMP. The present disclosure provides a method of treating cancer in an individual, the method comprising administering to the individual an effective amount of a TMMP of the present disclosure, or one or more nucleic acids (e.g., expression vectors; mRNA; etc.) comprising nucleotide sequences encoding the TMMP, where the TMMP comprises a T-cell epitope that is a cancer epitope, and where the TMMP comprises a stimulatory immunomodulatory polypeptide. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of cancer cells in the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of cancer cells in the individual by at least 10%, at least 15%, at least 20%,

at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to the number of cancer cells in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of cancer cells in the individual to undetectable levels.

[00561] In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the tumor mass in the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof (an individual having a tumor), reduces the tumor mass in the individual by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to the tumor mass in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof (an individual having a tumor), reduces the tumor volume in the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof (an individual having a tumor), reduces the tumor volume in the individual by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to the tumor volume in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, increases survival time of the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, increases survival time of the individual by at least 1 month, at least 2 months, at least 3 months, from 3 months to 6 months, from 6 months to 1 year, from 1 year to 2 years, from 2 years to 5 years, from 5 years to 10 years, or more than 10 years, compared to the expected survival time of the individual in the absence of administration with the TMMP.

[00562] In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a virus-infected cell, and contacting the epitope-specific T cell with the TMMP increases cytotoxic activity of the T cell toward the virus-infected cell. In some instances, the epitope-specific T cell is a T cell that is specific for an epitope present on a virus-infected cell, and contacting the epitope-specific T cell with the TMMP increases the number of the epitope-specific T cells.

[00563] Thus, the present disclosure provides a method of treating a virus infection in an individual, the method comprising administering to the individual an effective amount of a TMMP of the

present disclosure, or one or more nucleic acids comprising nucleotide sequences encoding the TMMP, where the TMMP comprises a T-cell epitope that is a viral epitope, and where the TMMP comprises a stimulatory immunomodulatory polypeptide. In some cases, an "effective amount" of a TMMP is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of virus-infected cells in the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of virus-infected cells in the individual by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to the number of virus-infected cells in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of virus-infected cells in the individual to undetectable levels.

[00564] Thus, the present disclosure provides a method of treating an infection in an individual, the method comprising administering to the individual an effective amount of a TMMP of the present disclosure, or one or more nucleic acids comprising nucleotide sequences encoding the TMMP, where the TMMP comprises a T-cell epitope that is a pathogen-associated epitope, and where the TMMP comprises a stimulatory immunomodulatory polypeptide. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of pathogens in the individual. For example, in some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of pathogens in the individual by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to the number of pathogens in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of pathogens in the individual to undetectable levels. Pathogens include viruses, bacteria, protozoans, and the like.

[00565] In some cases, the immunomodulatory polypeptide is an inhibitory polypeptide, and the TMMP inhibits activity of the epitope-specific T cell. In some cases, the epitope is a self-epitope, and the TMMP selectively inhibits the activity of a T cell specific for the self-epitope.

[00566] The present disclosure provides a method of treating an autoimmune disorder in an individual, the method comprising administering to the individual an effective amount of a TMMP of the present disclosure, or one or more nucleic acids comprising nucleotide sequences encoding the TMMP, where the TMMP comprises a T-cell epitope that is a self epitope, and where the TMMP comprises an

inhibitory immunomodulatory polypeptide. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number self-reactive T cells by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to number of self-reactive T cells in the individual before administration of the TMMP, or in the absence of administration with the TMMP. In some cases, an "effective amount" of a TMMP is an amount that, when administered in one or more doses to an individual in need thereof, reduces production of Th2 cytokines in the individual. In some cases, an "effective amount" of a TMMP of the present disclosure is an amount that, when administered in one or more doses to an individual in need thereof, ameliorates one or more symptoms associated with an autoimmune disease in the individual.

[00567] As noted above, in some cases, in carrying out a subject treatment method, a TMMP of the present disclosure is administered to an individual in need thereof, as the TMMP *per se*. In other instances, in carrying out a subject treatment method, one or more nucleic acids comprising nucleotide sequences encoding a TMMP of the present disclosure is/are administering to an individual in need thereof. Thus, in other instances, one or more nucleic acids of the present disclosure, e.g., one or more recombinant expression vectors of the present disclosure, is/are administered to an individual in need thereof.

Formulations

[00568] Suitable formulations are described above, where suitable formulations include a pharmaceutically acceptable excipient. In some cases, a suitable formulation comprises: a) a TMMP of the present disclosure; and b) a pharmaceutically acceptable excipient. In some cases, a suitable formulation comprises: a) a nucleic acid comprising a nucleotide sequence encoding a TMMP of the present disclosure; and b) a pharmaceutically acceptable excipient; in some instances, the nucleic acid is an mRNA. In some cases, a suitable formulation comprises: a) a first nucleic acid comprising a nucleotide sequence encoding the first polypeptide of a TMMP of the present disclosure; b) a second nucleic acid comprising a nucleotide sequence encoding the second polypeptide of a TMMP of the present disclosure; and c) a pharmaceutically acceptable excipient. In some cases, a suitable formulation comprises: a) a recombinant expression vector comprising a nucleotide sequence encoding a TMMP of the present disclosure; and b) a pharmaceutically acceptable excipient. In some cases, a suitable formulation comprises: a) a first recombinant expression vector comprising a nucleotide sequence encoding the first polypeptide of a TMMP of the present disclosure; b) a second recombinant expression vector comprising a nucleotide sequence encoding the second polypeptide of a TMMP of the present disclosure; and c) a pharmaceutically acceptable excipient.

[00569] Suitable pharmaceutically acceptable excipients are described above.

Dosages

[00570] A suitable dosage can be determined by an attending physician or other qualified medical personnel, based on various clinical factors. As is well known in the medical arts, dosages for any one patient depend upon many factors, including the patient's size, body surface area, age, the particular polypeptide or nucleic acid to be administered, sex of the patient, time, and route of administration, general health, and other drugs being administered concurrently. A TMMP of the present disclosure may be administered in amounts between 1 ng/kg body weight and 20 mg/kg body weight per dose, e.g. between 0.1 mg/kg body weight to 10 mg/kg body weight, e.g. between 0.5 mg/kg body weight to 5 mg/kg body weight; however, doses below or above this exemplary range are envisioned, especially considering the aforementioned factors. If the regimen is a continuous infusion, it can also be in the range of 1 μg to 10 mg per kilogram of body weight per minute. A TMMP of the present disclosure can be administered in an amount of from about 1 mg/kg body weight to 50 mg/kg body weight, e.g., from about 1 mg/kg body weight to about 5 mg/kg body weight, from about 5 mg/kg body weight to about 10 mg/kg body weight, from about 10 mg/kg body weight to about 15 mg/kg body weight, from about 15 mg/kg body weight to about 20 mg/kg body weight, from about 20 mg/kg body weight to about 25 mg/kg body weight, from about 25 mg/kg body weight to about 30 mg/kg body weight, from about 30 mg/kg body weight to about 35 mg/kg body weight, from about 35 mg/kg body weight to about 40 mg/kg body weight, or from about 40 mg/kg body weight to about 50 mg/kg body weight.

[00571] In some cases, a suitable dose of a TMMP of the present disclosure is from 0.01 μg to 100 g per kg of body weight, from 0.1 μg to 10 g per kg of body weight, from 1 μg to 1 g per kg of body weight, from 10 μg to 100 mg per kg of body weight, from 100 μg to 10 mg per kg of body weight, or from 100 μg to 1 mg per kg of body weight. Persons of ordinary skill in the art can easily estimate repetition rates for dosing based on measured residence times and concentrations of the administered agent in bodily fluids or tissues. Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein a TMMP of the present disclosure is administered in maintenance doses, ranging from 0.01 μg to 100 g per kg of body weight, from 0.1 μg to 10 g per kg of body weight, from 1 μg to 1 g per kg of body weight, from 10 μg to 100 mg per kg of body weight, from 100 μg to 10 mg per kg of body weight, or from 100 μg to 1 mg per kg of body weight.

[00572] Those of skill will readily appreciate that dose levels can vary as a function of the specific TMMP, the severity of the symptoms and the susceptibility of the subject to side effects. Preferred dosages for a given compound are readily determinable by those of skill in the art by a variety of means.

[00573] In some cases, multiple doses of a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure are administered. The frequency of administration of a TMMP of the present disclosure, a nucleic acid of the present

disclosure, or a recombinant expression vector of the present disclosure can vary depending on any of a variety of factors, e.g., severity of the symptoms, etc. For example, in some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered once per month, twice per month, three times per month, every other week (qow), once per week (qw), twice per week (biw), three times per week (tiw), four times per week, five times per week, six times per week, every other day (qod), daily (qd), twice a day (qid), or three times a day (tid).

[00574] The duration of administration of a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure, e.g., the period of time over which a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered, can vary, depending on any of a variety of factors, e.g., patient response, etc. For example, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure can be administered over a period of time ranging from about one day to about one week, from about two weeks to about four weeks, from about one month to about two months, from about two months to about four months, from about four months to about six months, from about six months to about eight months, from about eight months to about 1 year, from about 1 year to about 2 years, or from about 2 years to about 4 years, or more.

Routes of administration

[00575] An active agent (a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure) is administered to an individual using any available method and route suitable for drug delivery, including *in vivo* and *ex vivo* methods, as well as systemic and localized routes of administration.

[00576] Conventional and pharmaceutically acceptable routes of administration include intratumoral, peritumoral, intramuscular, intralymphatic, intratracheal, intracranial, subcutaneous, intradermal, topical application, intravenous, intraarterial, rectal, nasal, oral, and other enteral and parenteral routes of administration. Routes of administration may be combined, if desired, or adjusted depending upon the TMMP and/or the desired effect. A TMMP of the present disclosure, or a nucleic acid or recombinant expression vector of the present disclosure, can be administered in a single dose or in multiple doses.

[00577] In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered intravenously. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered intramuscularly. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the

present disclosure is administered intralymphatically. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered locally. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered intratumorally. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered peritumorally. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered intracranially. In some cases, a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered subcutaneously.

[00578] In some cases, a TMMP of the present disclosure is administered intravenously. In some cases, a TMMP of the present disclosure is administered intramuscularly. In some cases, a TMMP of the present disclosure is administered locally. In some cases, a TMMP the present disclosure is administered intratumorally. In some cases, a TMMP of the present disclosure is administered peritumorally. In some cases, a TMMP of the present disclosure is administered intracranially. In some cases, a TMMP is administered subcutaneously. In some cases, a TMMP of the present disclosure is administered intralymphatically.

[00579] A TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure can be administered to a host using any available conventional methods and routes suitable for delivery of conventional drugs, including systemic or localized routes. In general, routes of administration contemplated for use in a method of the present disclosure include, but are not necessarily limited to, enteral, parenteral, and inhalational routes.

[00580] Parenteral routes of administration other than inhalation administration include, but are not necessarily limited to, topical, transdermal, subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intratumoral, intralymphatic, peritumoral, and intravenous routes, *i.e.*, any route of administration other than through the alimentary canal. Parenteral administration can be carried to effect systemic or local delivery of a TMMP of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure. Where systemic delivery is desired, administration typically involves invasive or systemically absorbed topical or mucosal administration of pharmaceutical preparations.

Combination therapies

[00581] In some cases, a method of the present disclosure for treating cancer in an individual comprises: a) administering a TMMP of the present disclosure; and b) administering at least one additional therapeutic agent or therapeutic treatment. Suitable additional therapeutic agents include, but are not limited to, a small molecule cancer chemotherapeutic agent, and an immune checkpoint inhibitor.

Suitable additional therapeutic treatments include, e.g., radiation, surgery (e.g., surgical resection of a tumor), and the like.

[00582] A treatment method of the present disclosure can comprise co-administration of a TMMP of the present disclosure and at least one additional therapeutic agent. By "co-administration" is meant that both a TMMP of the present disclosure and at least one additional therapeutic agent are administered to an individual, although not necessarily at the same time, in order to achieve a therapeutic effect that is the result of having administered both the TMMP and the at least one additional therapeutic agent. The administration of the TMMP and the at least one additional therapeutic agent can be substantially simultaneous, e.g., the TMMP can be administered to an individual within about 1 minute to about 24 hours (e.g., within about 1 minute, within about 5 minutes, within about 15 minutes, within about 30 minutes, within about 1 hour, within about 4 hours, within about 8 hours, within about 12 hours, or within about 24 hours) of administration of the at least one additional therapeutic agent. In some cases, a TMMP of the present disclosure is administered to an individual who is undergoing treatment with, or who has undergone treatment with, the at least one additional therapeutic agent. The administration of the TMMP can occur at different times and/or at different frequencies.

[00583] As an example, a treatment method of the present disclosure can comprise co-administration of a TMMP of the present disclosure and an immune checkpoint inhibitor such as an antibody specific for an immune checkpoint. By "co-administration" is meant that both a TMMP of the present disclosure and an immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide) are administered to an individual, although not necessarily at the same time, in order to achieve a therapeutic effect that is the result of having administered both the TMMP and the immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide). The administration of the TMMP and the immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide) can be substantially simultaneous, e.g., the TMMP can be administered to an individual within about 1 minute to about 24 hours (e.g., within about 1 minute, within about 5 minutes, within about 15 minutes, within about 30 minutes, within about 1 hour, within about 4 hours, within about 8 hours, within about 12 hours, or within about 24 hours) of administration of the immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide). In some cases, a TMMP of the present disclosure is administered to an individual who is undergoing treatment with, or who has undergone treatment with, an immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide). The administration of the TMMP and the immune checkpoint inhibitor (e.g., an antibody specific for an immune checkpoint polypeptide) can occur at different times and/or at different frequencies.

[00584] Exemplary immune checkpoint inhibitors include inhibitors that target an immune checkpoint polypeptide such as CD27, CD28, CD40, CD122, CD96, CD73, CD47, OX40, GITR,

CSF1R, JAK, PI3K delta, PI3K gamma, TAM, arginase, CD137 (also known as 4-1BB), ICOS, A2AR, B7-H3, B7-H4, BTLA, CTLA-4, LAG3, TIM3, VISTA, CD96, TIGIT, CD122, PD-1, PD-L1 and PD-L2. In some cases, the immune checkpoint polypeptide is a stimulatory checkpoint molecule selected from CD27, CD28, CD40, ICOS, OX40, GITR, CD122 and CD137. In some cases, the immune checkpoint polypeptide is an inhibitory checkpoint molecule selected from A2AR, B7-H3, B7-H4, BTLA, CTLA-4, IDO, KIR, LAG3, PD-1, TIM3, CD96, TIGIT and VISTA.

[00585] In some cases, the immune checkpoint inhibitor is an antibody specific for an immune checkpoint polypeptide. In some cases, the anti-immune checkpoint antibody is a monoclonal antibody. In some cases, the anti-immune checkpoint antibody is humanized, or de-immunized such that the antibody does not substantially elicit an immune response in a human. In some cases, the anti-immune checkpoint antibody is a humanized monoclonal antibody. In some cases, the anti-immune checkpoint antibody is a de-immunized monoclonal antibody. In some cases, the anti-immune checkpoint antibody is a fully human monoclonal antibody. In some cases, the anti-immune checkpoint antibody inhibits binding of the immune checkpoint polypeptide to a ligand for the immune checkpoint polypeptide. In some cases, the anti-immune checkpoint antibody inhibits binding of the immune checkpoint polypeptide to a receptor for the immune checkpoint polypeptide.

[00586] Suitable anti-immune checkpoint antibodies include, but are not limited to, nivolumab (Bristol-Myers Squibb), pembrolizumab (Merck), pidilizumab (Curetech), AMP-224 (GlaxoSmithKline/Amplimmune), MPDL3280A (Roche), MDX-1105 (Medarex, Inc./Bristol Myer Squibb), MEDI-4736 (Medimmune/AstraZeneca), arelumab (Merck Serono), ipilimumab (YERVOY, (Bristol-Myers Squibb), tremelimumab (Pfizer), pidilizumab (CureTech, Ltd.), IMP321 (Immutep S.A.), MGA271 (Macrogenics), BMS-986016 (Bristol-Meyers Squibb), lirilumab (Bristol-Myers Squibb), urelumab (Bristol-Meyers Squibb), PF-05082566 (Pfizer), IPH2101 (Innate Pharma/Bristol-Myers Squibb), MEDI-6469 (MedImmune/AZ), CP-870,893 (Genentech), Mogamulizumab (Kyowa Hakko Kirin), Varlilumab (CelIDex Therapeutics), Avelumab (EMD Serono), Galiximab (Biogen Idec), AMP-514 (Amplimmune/AZ), AUNP 12 (Aurigene and Pierre Fabre), Indoximod (NewLink Genetics), NLG-919 (NewLink Genetics), INCB024360 (Incyte); KN035; and combinations thereof. For example, in some cases, the immune checkpoint inhibitor is an anti-PD-1 antibody. Suitable anti-PD-1 antibodies include, e.g., nivolumab, pembrolizumab (also known as MK-3475), pidilizumab, SHR-1210, PDR001, and AMP-224. In some cases, the anti-PD-1 monoclonal antibody is nivolumab, pembrolizumab or PDR001. Suitable anti-PD1 antibodies are described in U.S. Patent Publication No. 2017/0044259. For pidilizumab, see, e.g., Rosenblatt et al. (2011) J. Immunother. 34:409-18. In some cases, the immune checkpoint inhibitor is an anti-CTLA-4 antibody. In some cases, the anti-CTLA-4 antibody is ipilimumab or tremelimumab. For tremelimumab, see, e.g., Ribas et al. (2013) J. Clin. Oncol. 31:616-22. In some cases, the immune checkpoint inhibitor is an anti-PD-L1 antibody. In some cases, the anti-PD-

L1 monoclonal antibody is BMS-935559, MEDI4736, MPDL3280A (also known as RG7446), KN035, or MSB0010718C. In some embodiments, the anti-PD-L1 monoclonal antibody is MPDL3280A (atezolizumab) or MEDI4736 (durvalumab). For durvalumab, see, e.g., WO 2011/066389. For atezolizumab, see, e.g., U.S. Patent No. 8,217,149.

Subjects suitable for treatment

[00587] Subjects suitable for treatment with a method of the present disclosure include individuals who have cancer, including individuals who have been diagnosed as having cancer, individuals who have been treated for cancer but who failed to respond to the treatment, and individuals who have been treated for cancer and who initially responded but subsequently became refractory to the treatment. Subjects suitable for treatment with a method of the present disclosure include individuals who have an infection (e.g., an infection with a pathogen such as a bacterium, a virus, a protozoan, etc.), including individuals who have been diagnosed as having an infection, and individuals who have been treated for an infection but who failed to respond to the treatment. Subjects suitable for treatment with a method of the present disclosure include individuals who have bacterial infection, including individuals who have been diagnosed as having a bacterial infection, and individuals who have been treated for a bacterial infection but who failed to respond to the treatment. Subjects suitable for treatment with a method of the present disclosure include individuals who have a viral infection, including individuals who have been diagnosed as having a viral infection, and individuals who have been treated for a viral infection but who failed to respond to the treatment. Subjects suitable for treatment with a method of the present disclosure include individuals who have an autoimmune disease, including individuals who have been diagnosed as having an autoimmune disease, and individuals who have been treated for an autoimmune disease but who failed to respond to the treatment.

Examples of Non-Limiting Aspects of the Disclosure

[00588] Aspects, including embodiments, of the present subject matter described above may be beneficial alone or in combination, with one or more other aspects or embodiments. Without limiting the foregoing description, certain non-limiting aspects of the disclosure numbered 1-95 are provided below. As will be apparent to those of skill in the art upon reading this disclosure, each of the individually numbered aspects may be used or combined with any of the preceding or following individually numbered aspects. This is intended to provide support for all such combinations of aspects and is not limited to combinations of aspects explicitly provided below:

[00589] Aspect 1. A T-cell modulatory multimeric polypeptide comprising: at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope, wherein the peptide has a length of at least 4 amino acids; and ii) first major histocompatibility complex (MHC) polypeptide; b) a second polypeptide comprising a second MHC polypeptide, and c) at least one immunomodulatory

polypeptide, wherein the first and/or the second polypeptide comprises the immunomodulatory polypeptide.

[00590] Aspect 2. T-cell modulatory multimeric polypeptide of aspect 1, wherein at least one of the one or more immunomodulatory domains is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide, and wherein the epitope binds to a T-cell receptor (TCR) on a T cell with an affinity of at least 10^{-7} M, such that: i) the T-cell modulatory multimeric polypeptide binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the T-cell modulatory multimeric polypeptide binds a second T cell, wherein the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 10^{-7} M, and wherein the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 10^{-7} M; and/or ii) the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is in a range of from 1.5:1 to 10^6:1.

[00591] Aspect 3. A T-cell modulatory multimeric polypeptide of aspect 2, wherein: a) the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold higher than the affinity with which it binds the second T cell; and/or b) the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-7} M, from about 10^{-4} M to about 10^{-6} M, from about 10^{-4} M to about 10^{-5} M; and/or c) wherein the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is at least 10:1, at least 50:1, at least 10^2:1, or at least 10^3:1.

[00592] Aspect 4. A T-cell modulatory multimeric polypeptide of any one of aspects 1-3, wherein the first or the second polypeptide comprises an immunoglobulin (Ig) Fc polypeptide.

[00593] Aspect 5. A T-cell modulatory multimeric polypeptide of aspect 4, wherein the Ig Fc polypeptide is an IgG1 Fc polypeptide.

[00594] Aspect 6. A T-cell modulatory multimeric polypeptide of aspect 5, wherein IgG1 Fc polypeptide comprises one or more amino acid substitutions selected from N297A, L234A, L235A, L234F, L235E, and P331S.

[00595] Aspect 7. A T-cell modulatory multimeric polypeptide of any one of aspects 1-6, wherein:

[00596] a1) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; ii) the first MHC polypeptide; and iii) at least one immunomodulatory polypeptide; and b1) the second polypeptide comprises, in order from N-terminus to C-terminus: i) the second MHC polypeptide; and ii) an immunoglobulin (Ig) Fc polypeptide; or

[00597] a2) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; and ii) the first MHC polypeptide; and b2) the second polypeptide comprises, in order from N-terminus to C-terminus: i) at least one immunomodulatory polypeptide; ii) the second MHC polypeptide; and iii) an Ig Fc polypeptide; or

[00598] a3) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; and ii) the first MHC polypeptide; and b3) the second polypeptide comprises, in order from N-terminus to C-terminus: i) the second MHC polypeptide; and ii) an Ig Fc polypeptide; and iii) at least one immunomodulatory polypeptide; or

[00599] a4) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; and ii) the first MHC polypeptide; and b4) the second polypeptide comprises, in order from N-terminus to C-terminus: i) the second MHC polypeptide; and ii) at least one immunomodulatory polypeptide; or

[00600] a5) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; and ii) the first MHC polypeptide; and b5) a second polypeptide comprises, in order from N-terminus to C-terminus: i) at least one immunomodulatory polypeptide; and ii) the second MHC polypeptide; or

[00601] a6) the first polypeptide comprises, in order from N-terminus to C-terminus: i) the peptide epitope; ii) the first MHC polypeptide; and iii) at least one immunomodulatory polypeptide; and b6) the second polypeptide comprises: i) the second MHC polypeptide.

[00602] Aspect 8. A T-cell modulatory multimeric polypeptide of any one of aspects 1-7, wherein the first polypeptide comprises a peptide linker between the epitope and the first MHC polypeptide and/or wherein the second polypeptide comprises a peptide linker between the immunomodulatory polypeptide and the second MHC polypeptide.

[00603] Aspect 9. A T-cell modulatory multimeric polypeptide of aspect 8, wherein the peptide linker comprises the amino acid sequence (GGGGS)n, where n is an integer from 1 to 10.

[00604] Aspect 10. A T-cell modulatory multimeric polypeptide of any one of aspects 1-9, wherein the first MHC polypeptide is a β2-microglobulin polypeptide; and wherein the second MHC polypeptide is an MHC class I heavy chain polypeptide.

[00605] Aspect 11. A T-cell modulatory multimeric polypeptide of any one of aspects 1-10, wherein the at least one immunomodulatory polypeptide is selected from the group consisting of a cytokine (e.g., an IL2 polypeptide, an IL7 polypeptide, an IL12 polypeptide, an IL15 polypeptide, an IL17 polypeptide, an IL21 polypeptide, an IL27 polypeptide, an IL-23 polypeptide, a TGFβ polypeptide, and the like; and including all family members, e.g., IL17A, IL-17B, IL-17C, IL-17D, IL-17E, IL-17F, IL-17E), a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, a CD40 polypeptide, a CD70 polypeptide, a JAG1 (CD339) polypeptide, an ICAM (CD540 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a PD-L2 polypeptide, a PD-1H (VISTA) polypeptide, an ICOS-L (CD275) polypeptide, a GITRL polypeptide, an HVEM polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, a Galectin-9 polypeptide, a CD83 polypeptide, a CD30L polypeptide, a HLA-G polypeptide, a MICA polypeptide, a MICB polypeptide, a HVEM (CD270) polypeptide, a lymphotoxin beta receptor polypeptide, a 3/TR6 polypeptide, an ILT3 polypeptide, an ILT4 polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, and combinations thereof.

[00606] Aspect 12. A T-cell modulatory multimeric polypeptide of any one of aspects 1-11, wherein the at least one immunomodulatory polypeptide is an IL-2 polypeptide.

[00607] Aspect 13. A T-cell modulatory multimeric polypeptide of any one of aspects 1-12, wherein the multimeric polypeptide comprises at least two immunomodulatory polypeptides, and wherein at least two of the immunomodulatory polypeptides are the same.

[00608] Aspect 14. A T-cell modulatory multimeric polypeptide of aspect 13, wherein the 2 or more immunomodulatory polypeptides are in tandem.

[00609] Aspect 15. A T-cell modulatory multimeric polypeptide of any one of aspects 1-14, wherein the first polypeptide and the second polypeptide are covalently linked to one another.

[00610] Aspect 16. A T-cell modulatory multimeric polypeptide of aspect 15, wherein the covalent linkage is via a disulfide bond.

[00611] Aspect 17. A T-cell modulatory multimeric polypeptide of any one of aspects 1-16, wherein the first MHC polypeptide or a linker between the epitope and the first MHC polypeptide comprises an amino acid substitution to provide a first Cys residue, wherein the second MHC polypeptide comprises an amino acid substitution to provide a second Cys residue, and wherein the disulfide linkage is between the first and the second Cys residues.

[00612] Aspect 18. A T-cell modulatory multimeric polypeptide of any one of aspects 1-17, wherein the peptide epitope has a length of from about 4 amino acids to about 25 amino acids.

[00613] Aspect 19. A T-cell modulatory multimeric polypeptide of any one of aspects 1-18, wherein the peptide epitope is a cancer epitope.

[00614] Aspect 20. A T-cell modulatory multimeric polypeptide of any one of aspects 1-18, wherein the peptide epitope is a viral epitope.

[00615] Aspect 21. A T-cell modulatory multimeric polypeptide of any one of aspects 1-20, wherein the first or the second MHC polypeptide comprises: a) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-A*0101, HLA-A*0201, HLA-A*0201, HLA-A*1101, HLA-A*2301, HLA-A*2402, HLA-A*2407, HLA-A*3303, or HLA-A*3401 amino acid sequence depicted in FIG. 7A; or b) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-B*0702, HLA-B*0801, HLA-B*1502, HLA-B*3802, HLA-B*4001, HLA-B*4601, or HLA-B*5301 amino acid sequence depicted in FIG. 8A; or c) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-C*0102, HLA-C*0303, HLA-C*0304, HLA-C*0401, HLA-C*0602, HLA-C*0701, HLA-C*0702, HLA-C*0801, or HLA-C*1502 depicted in FIG. 9A.

[00616] Aspect 22. A T-cell modulatory multimeric polypeptide of any one of aspects 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*2402 polypeptide.

[00617] Aspect 23. A T-cell modulatory multimeric polypeptide of any one of aspects 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide is an HLA-A*1101 polypeptide.

[00618] Aspect 24. A T-cell modulatory multimeric polypeptide of any one of aspects 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*3303 polypeptide.

[00619] Aspect 25. A T-cell modulatory multimeric polypeptide of any one of aspects 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*0201 polypeptide.

[00620] Aspect 26. A T-cell modulatory multimeric polypeptide of any one of aspects 21-25, wherein the MHC heavy chain polypeptide comprises a Cys at position 236.

[00621] Aspect 27. A T-cell modulatory multimeric polypeptide of any one of aspects 21-26, wherein the β2M polypeptide comprises a Cys at position 12.

[00622] Aspect 28. A T-cell modulatory multimeric polypeptide of any one of aspects 1-27, wherein the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising: i) an H16A substitution and an F42A substation; or ii) an H16T substitution and an F42A substitution.

[00623] Aspect 29. A T-cell modulatory multimeric polypeptide of any one of aspects 1-28, wherein the multimeric polypeptide comprises a first and a second heterodimer, and wherein the first and second heterodimers are covalently bound by one or more disulfide bonds between the Ig Fc polypeptides of the first and second heterodimers.

[00624] Aspect 30. A nucleic acid comprising a nucleotide sequence encoding a first or second polypeptide according to any one of aspects 1-28, wherein the first or second polypeptide comprises at least one immunomodulatory domain.

[00625] Aspect 31. An expression vector comprising the nucleic acid of aspect 30.

[00626] Aspect 32. A method of selectively modulating the activity of T cell specific for a given epitope, the method comprising contacting the T cell with a T-cell modulatory multimeric polypeptide according to any one of aspects 1-29, wherein said contacting selectively modulates the activity of the epitope-specific T cell.

[00627] Aspect 33. A method of treating a patient having a cancer, the method comprising administering to the patient an effective amount of a pharmaceutical composition comprising T-cell modulatory multimeric polypeptide according to any one of aspects 1-29.

[00628] Aspect 34. The method of aspect 33, wherein the cancer is cervical cancer, prostate cancer, or ovarian cancer.

[00629] Aspect 35. The method of aspect 33 or 34, wherein said administering is intramuscular.

[00630] Aspect 36. The method of aspect 33 or 34, wherein said administering is intravenous.

[00631] Aspect 37. A method of modulating an immune response in an individual, the method comprising administering to the individual an effective amount of the T-cell modulatory multimeric polypeptide (TMMP) of any one of aspects 12927, wherein said administering induces an epitope-specific T cell response (e.g., a T cell response specific for the epitope present in the TMMP) and an epitope-non-specific T cell response, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 2:1.

[00632] Aspect 38. The method of aspect 37, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 5:1.

[00633] Aspect 39. The method of aspect 37, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 10:1.

[00634] Aspect 40. The method of aspect 37, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 25:1.

[00635] Aspect 41. The method of aspect 37, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 50:1.

[00636] Aspect 42. The method of aspect 37, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 100:1.

[00637] Aspect 43. The method of any one of aspects 37-42, wherein the individual is a human.

[00638] Aspect 44. The method of any one of aspects 37-43, wherein said modulating comprises increasing a cytotoxic T-cell response to a cancer cell (e.g., a cancer cell expressing the peptide epitope present in the TMMP).

[00639] Aspect 45. The method of any one of aspects 37-44, wherein said administering is intravenous, subcutaneous, intramuscular, systemic, intralymphatic, distal to a treatment site, local, or at or near a treatment site.

[00640] Aspect 47. The method of any one of aspects 37-45, wherein the epitope non-specific T-cell response is less than the epitope non-specific T-cell response that would be induced by a control T-cell modulatory multimeric polypeptide comprising a corresponding wild-type immunomodulatory polypeptide.

[00641] Aspect 48. A method of delivering a costimulatory (i.e., immunomodulatory) polypeptide selectively to target T cell, the method comprising contacting a mixed population of T cells with a T-cell modulatory multimeric polypeptide (TMMP) of any one of aspects 1-29, wherein the mixed population of T cells comprises the target T cell and non-target T cells, wherein the target T cell is specific for the epitope present within the TMMP (e.g., wherein the target T cell is specific for the epitope present within the TMMP), and wherein said contacting delivers the one or more costimulatory polypeptides present within the TMMP to the target T cell.

[00642] Aspect 49. The method of aspect 48, wherein the population of T cells is *in vitro*.

[00643] Aspect 50. The method of aspect 48, wherein the population of T cells is *in vivo* in an individual.

[00644] Aspect 51. The method of aspect 50, comprising administering the multimeric polypeptide to the individual.

[00645] Aspect 52. The method of any one of aspects 48-51, wherein the target T cell is a cytotoxic T cell.

[00646] Aspect 53. The method of aspect 48, wherein the mixed population of T cells is an *in vitro* population of mixed T cells obtained from an individual, and wherein said contacting results in activation and/or proliferation of the target T cell, generating a population of activated and/or proliferated target T cells.

[00647] Aspect 54. The method of aspect 53, further comprising administering the population of activated and/or proliferated target T cells to the individual.

[00648] Aspect 55. A method of detecting, in a mixed population of T cells obtained from an individual, the presence of a target T cell that binds an epitope of interest, the method comprising: a) contacting *in vitro* the mixed population of T cells with T-cell modulatory multimeric polypeptide (TMMP) of any one of aspects 1-29, wherein the TMMP comprises the epitope of interest; and b) detecting activation and/or proliferation of T cells in response to said contacting, wherein activated and/or proliferated T cells indicates the presence of the target T cell.

[00649] Aspect 56. A T-cell modulatory multimeric polypeptide comprising: at least one heterodimer comprising: a) a first polypeptide comprising: i) a peptide epitope, wherein the peptide has a length of from about 4 amino acids to about 25 amino acids; and ii) first major histocompatibility complex (MHC) class I polypeptide; b) a second polypeptide comprising a second MHC class I polypeptide, and c) at least one immunomodulatory polypeptide, wherein the first and/or the second polypeptide comprises the immunomodulatory polypeptide, and wherein the first and the second polypeptides are covalently linked to one another via at least 2 disulfide bonds.

[00650] Aspect 57. A T-cell modulatory multimeric polypeptide of aspect 56, wherein at least one of the at least one immunomodulatory polypeptides is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide, and wherein the epitope binds to a T-cell receptor (TCR) on a T cell with an affinity of at least 10^{-7} M, such that: i) the T-cell modulatory multimeric polypeptide binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the T-cell modulatory multimeric polypeptide binds a second T cell, wherein the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 10^{-7} M, and wherein the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 10^{-7} M; and/or ii) the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is in a range of from 1.5:1 to 10^6:1.

[00651] Aspect 58. A T-cell modulatory multimeric polypeptide of aspect 57, wherein: a) the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold higher than the affinity with which it binds the second T

cell; and/or b) the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-7} M, from about 10^{-4} M to about 10^{-6} M, from about 10^{-4} M to about 10^{-5} M; and/or c) wherein the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is at least 10:1, at least 50:1, at least 10^2:1, or at least 10^3:1.

[00652] Aspect 59. A T-cell modulatory multimeric polypeptide of any one of aspects 56-58, wherein the first or the second polypeptide comprises an immunoglobulin (Ig) Fc polypeptide.

[00653] Aspect 60. A T-cell modulatory multimeric polypeptide of aspect 59, wherein the Ig Fc polypeptide is an IgG1 Fc polypeptide.

[00654] Aspect 61. A T-cell modulatory multimeric polypeptide of aspect 59, wherein the Ig Fc polypeptide is an IgG4 Fc polypeptide.

[00655] Aspect 62. A T-cell modulatory multimeric polypeptide of aspect 60, wherein IgG1 Fc polypeptide comprises one or more amino acid substitutions selected from N297A, L234A, L235A, L234F, L235E, and P331S.

[00656] Aspect 63. A T-cell modulatory multimeric polypeptide of any one of aspects 56-62, wherein

a1) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope;

ii) the first class I MHC polypeptide; and

iii) at least one immunomodulatory polypeptide; and

b1) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second class I MHC polypeptide; and

ii) an immunoglobulin (Ig) Fc polypeptide; or

a2) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first class I MHC polypeptide; and

b2) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) at least one immunomodulatory polypeptide;

ii) the second class I MHC polypeptide; and

iii) an Ig Fc polypeptide; or

a3) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first class I MHC polypeptide; and

b3) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second class I MHC polypeptide; and

ii) an Ig Fc polypeptide; and

iii) at least one immunomodulatory polypeptide; or

a4) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first class I MHC polypeptide; and

b4) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second class I MHC polypeptide; and

ii) at least one immunomodulatory polypeptide; or

a5) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first class I MHC polypeptide; and

b5) a second polypeptide comprises, in order from N-terminus to C-terminus:

i) at least one immunomodulatory polypeptide; and

ii) the second class I MHC polypeptide; or

a6) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope;

ii) the first class I MHC polypeptide; and

iii) at least one immunomodulatory polypeptide; and

b6) the second polypeptide comprises:

i) the second class I MHC polypeptide.

[00657] Aspect 64. A T-cell modulatory multimeric polypeptide of any one of aspects 56-63, wherein the first MHC polypeptide is a β2-microglobulin polypeptide; and wherein the second MHC polypeptide is an MHC class I heavy chain polypeptide.

[00658] Aspect 65. A T-cell modulatory multimeric polypeptide of any one of aspects 56-64, wherein the at least one immunomodulatory polypeptide is selected from the group consisting of a cytokine (e.g., an IL2 polypeptide, an IL7 polypeptide, an IL12 polypeptide, an IL15 polypeptide, an IL17 polypeptide, an IL21 polypeptide, an IL27 polypeptide, an IL-23 polypeptide, a TGFβ polypeptide, and the like; and including all family members, e.g., IL17A, IL-17B, IL-17C, IL-17D, IL-17E, IL-17F, IL-17E), a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, a CD40 polypeptide, a CD70 polypeptide, a JAG1 (CD339) polypeptide, an ICAM (CD540 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a PD-L2 polypeptide, a PD-1H (VISTA)

polypeptide, an ICOS-L (CD275) polypeptide, a GITRL polypeptide, an HVEM polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, a Galectin-9 polypeptide, a CD83 polypeptide, a CD30L polypeptide, a HLA-G polypeptide, a MICA polypeptide, a MICB polypeptide, a HVEM (CD270) polypeptide, a lymphotoxin beta receptor polypeptide, a 3/TR6 polypeptide, an ILT3 polypeptide, an ILT4 polypeptide, a CXCL10 polypeptide, a CXCL9 polypeptide, a CXCL11 polypeptide, a CXCL13 polypeptide, and a CX3CL1 polypeptide, and combinations thereof.

[00659] Aspect 66. A T-cell modulatory multimeric polypeptide of any one of aspects 56-64, wherein the at least one immunomodulatory polypeptide is an IL-2 polypeptide.

[00660] Aspect 67. A T-cell modulatory multimeric polypeptide of any one of aspects 56-66, wherein the multimeric polypeptide comprises at least two immunomodulatory polypeptides, and wherein at least two of the immunomodulatory polypeptides are the same.

[00661] Aspect 68. A T-cell modulatory multimeric polypeptide of aspect 67, wherein the 2 or more immunomodulatory polypeptides are in tandem.

[00662] Aspect 69. The T-cell modulatory multimeric polypeptide of any one of aspects 56-68, wherein: a) a first disulfide bond is between: i) a Cys present in a linker between the peptide epitope and the first MHC class I polypeptide, wherein the first MHC class I polypeptide is a β2M polypeptide; and ii) a Cys residue introduced via a Y84C substitution in the second MHC class I polypeptide, wherein the second MHC class I polypeptide is a MHC Class I heavy chain polypeptide; and b) a second disulfide bond is between: i) a Cys residue introduced into the β2M polypeptide via an R12C substitution; and ii) a Cys residue introduced into the MHC Class I heavy chain polypeptide via an A236C substitution.

[00663] Aspect 70. A T-cell modulatory multimeric polypeptide of aspect 69, wherein the linker comprises the amino acid sequence GCGGS (SEQ ID NO:318).

[00664] Aspect 71. A T-cell modulatory multimeric polypeptide of aspect 70, wherein the linker comprises the amino acid sequence GCGGS(GGGGS)n (SEQ ID NO:342), where n is an integer from 1 to 10.

[00665] Aspect 72. A T-cell modulatory multimeric polypeptide of any one of aspects 56-71, wherein the peptide epitope is a cancer-associated peptide epitope.

[00666] Aspect 73. A T-cell modulatory multimeric polypeptide of any one of aspects 56-71, wherein the peptide epitope is a virus-associated peptide epitope.

[00667] Aspect 74. A T-cell modulatory multimeric polypeptide of any one of aspects 56-73, wherein the first or the second MHC polypeptide comprises: a) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-A*0101, HLA-A*0201, HLA-A*0201, HLA-A*1101, HLA-A*2301, HLA-A*2402, HLA-A*2407, HLA-A*3303, or HLA-A*3401 amino acid sequence

depicted in FIG. 7A; or b) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-B*0702, HLA-B*0801, HLA-B*1502, HLA-B*3802, HLA-B*4001, HLA-B*4601, or HLA-B*5301 amino acid sequence depicted in FIG. 8A; or c) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-C*0102, HLA-C*0303, HLA-C*0304, HLA-C*0401, HLA-C*0602, HLA-C*0701, HLA-C*0702, HLA-C*0801, or HLA-C*1502 depicted in FIG. 9A.

[00668] Aspect 75. A T-cell modulatory multimeric polypeptide of any one of aspects 56-73, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*2402 polypeptide.

[00669] Aspect 76. A T-cell modulatory multimeric polypeptide of any one of aspects 56-73, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide is an HLA-A*1101 polypeptide.

[00670] Aspect 77. A T-cell modulatory multimeric polypeptide of any one of aspects 56-73, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*3303 polypeptide.

[00671] Aspect 78. A T-cell modulatory multimeric polypeptide of any one of aspects 56-73, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*0201 polypeptide.

[00672] Aspect 79. A T-cell modulatory multimeric polypeptide of any one of aspects 56-78, wherein the MHC heavy chain polypeptide comprises a Cys at position 236.

[00673] Aspect 80. A T-cell modulatory multimeric polypeptide of any one of aspects 56-79, wherein the β2M polypeptide comprises a Cys at position 12.

[00674] Aspect 81. A T-cell modulatory multimeric polypeptide of any one of aspects 56-80, wherein the immunomodulatory polypeptide is a variant IL-2 polypeptide comprising: i) an H16A substitution and an F42A substation; or ii) an H16T substitution and an F42A substitution.

[00675] Aspect 82. A T-cell modulatory multimeric polypeptide of any one of aspects 56-81, wherein the multimeric polypeptide comprises a first and a second heterodimer, and wherein the first and second heterodimers are covalently bound by one or more disulfide bonds between the Ig Fc polypeptides of the first and second heterodimers.

[00676] Aspect 83. A nucleic acid comprising a nucleotide sequence encoding a first or second polypeptide according to any one of aspects 56-82, wherein the first or second polypeptide comprises at least one immunomodulatory domain.

[00677] Aspect 84. An expression vector comprising the nucleic acid of aspect 83.

[00678] Aspect 85. A method of selectively modulating the activity of T cell specific for a peptide epitope, the method comprising contacting the T cell with a T-cell modulatory multimeric polypeptide according to any one of aspects 56-82, wherein said contacting selectively modulates the activity of the epitope-specific T cell.

[00679] Aspect 86. A method of treating a patient having a cancer, the method comprising administering to the patient an effective amount of a pharmaceutical composition comprising T-cell modulatory multimeric polypeptide according to any one of aspects 56-82.

[00680] Aspect 87. The method of aspect 86, wherein said administering is intramuscular.

[00681] Aspect 88. The method of aspect 86, wherein said administering is intravenous.

[00682] Aspect 89. A method of any one of aspects 86-88, further comprising administering one or more checkpoint inhibitors to the individual.

[00683] Aspect 90. A method according to aspect 89, wherein the checkpoint inhibitor is an antibody that binds to a polypeptide selected from the group consisting of CD27, CD28, CD40, CD122, CD96, CD73, CD47, OX40, GITR, CSF1R, JAK, PI3K delta, PI3K gamma, TAM, arginase, CD137, ICOS, A2AR, B7-H3, B7-H4, BTLA, CTLA-4, LAG3, TIM3, VISTA, CD96, TIGIT, CD122, PD-1, PD-L1, and PD-L2.

[00684] Aspect 91. A method according to aspect 89, wherein the checkpoint inhibitor is an antibody specific for PD-1, PD-L1, or CTLA4.

[00685] Aspect 92. A method according to aspect 89, wherein the one or more checkpoint inhibitors is selected from the group consisting of nivolumab, pembrolizumab, pidilizumab, AMP-224, MPDL3280A, MDX-1105, MEDI-4736, arelumab, ipilimumab, tremelimumab, pidilizumab, IMP321, MGA271, BMS-986016, lirilumab, urelumab, PF-05082566, IPH2101, MEDI-6469, CP-870,893, Mogamulizumab, Varlilumab, Avelumab, Galiximab, AMP-514, AUNP 12, Indoximod, NLG-919, INCB024360, KN035, and combinations thereof.

[00686] Aspect 93. A method of modulating an immune response in an individual, the method comprising administering to the individual an effective amount of the T-cell modulatory multimeric polypeptide of any one of aspects 56-82, wherein said administering induces an epitope-specific T cell response and an epitope-non-specific T cell response, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 2:1.

[00687] Aspect 94. A method of delivering an immunomodulatory polypeptide selectively to a target T cell, the method comprising contacting a mixed population of T cells with a T-cell modulatory multimeric polypeptide of any one of aspects 56-82, wherein the mixed population of T cells comprises the target T cell and non-target T cells, wherein the target T cell is specific for the epitope present within

the T-cell modulatory multimeric polypeptide, and wherein said contacting delivers the one or more immunomodulatory polypeptides present within the T-cell modulatory multimeric polypeptide to the target T cell.

[00688] Aspect 95. A method of detecting, in a mixed population of T cells obtained from an individual, the presence of a target T cell that binds a peptide epitope, the method comprising: a) contacting *in vitro* the mixed population of T cells with the T-cell modulatory multimeric polypeptide of any one of aspects 56-82, wherein the T-cell modulatory multimeric polypeptide comprises the peptide epitope; and b) detecting activation and/or proliferation of T cells in response to said contacting, wherein activated and/or proliferated T cells indicates the presence of the target T cell.

[00689] While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

CLAIMS

What is claimed is:

1. A T-cell modulatory multimeric polypeptide comprising:

at least one heterodimer comprising:

a) a first polypeptide comprising:

i) a peptide epitope, wherein the peptide has a length of at least 4 amino acids; and

ii) first major histocompatibility complex (MHC) polypeptide;

b) a second polypeptide comprising a second MHC polypeptide, and

c) at least one immunomodulatory polypeptide,

wherein the first and/or the second polypeptide comprises the immunomodulatory polypeptide.

2. A T-cell modulatory multimeric polypeptide of claim 1, wherein at least one of the at least one immunomodulatory polypeptide is a variant immunomodulatory polypeptide that exhibits reduced affinity to a cognate co-immunomodulatory polypeptide compared to the affinity of a corresponding wild-type immunomodulatory polypeptide for the cognate co-immunomodulatory polypeptide,

and wherein the epitope binds to a T-cell receptor (TCR) on a T cell with an affinity of at least 10^{-7} M,

such that:

i) the T-cell modulatory multimeric polypeptide binds to a first T cell with an affinity that is at least 25% higher than the affinity with which the T-cell modulatory multimeric polypeptide binds a second T cell,

wherein the first T cell expresses on its surface the cognate co-immunomodulatory polypeptide and a TCR that binds the epitope with an affinity of at least 10^{-7} M, and

wherein the second T cell expresses on its surface the cognate co-immunomodulatory polypeptide but does not express on its surface a TCR that binds the epitope with an affinity of at least 10^{-7} M; and/or

ii) the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-

immunomodulatory polypeptide, when measured by bio-layer interferometry, is in a range of from 1.5:1 to 10^6:1.

3. A T-cell modulatory multimeric polypeptide of claim 2, wherein:

a) the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 50%, at least 2-fold, at least 5-fold, or at least 10-fold higher than the affinity with which it binds the second T cell; and/or

b) the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-7} M, from about 10^{-4} M to about 10^{-6} M, from about 10^{-4} M to about 10^{-5} M; and/or

c) wherein the ratio of the binding affinity of a control T-cell modulatory multimeric polypeptide, wherein the control comprises a wild-type immunomodulatory polypeptide, to a cognate co-immunomodulatory polypeptide to the binding affinity of the T-cell modulatory multimeric polypeptide comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is at least 10:1, at least 50:1, at least 10^2:1, or at least 10^3:1.

4. A T-cell modulatory multimeric polypeptide of any one of claims 1-3, wherein

a1) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope;

ii) the first MHC polypeptide; and

iii) at least one immunomodulatory polypeptide; and

b1) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second MHC polypeptide; and

ii) an immunoglobulin (Ig) Fc polypeptide; or

a2) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first MHC polypeptide; and

b2) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) at least one immunomodulatory polypeptide;

ii) the second MHC polypeptide; and

iii) an Ig Fc polypeptide; or

a3) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first MHC polypeptide; and

b3) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second MHC polypeptide; and

ii) an Ig Fc polypeptide; and

iii) at least one immunomodulatory polypeptide; or

a4) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first MHC polypeptide; and

b4) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the second MHC polypeptide; and

ii) at least one immunomodulatory polypeptide; or

a5) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the first MHC polypeptide; and

b5) a second polypeptide comprises, in order from N-terminus to C-terminus:

i) at least one immunomodulatory polypeptide; and

ii) the second MHC polypeptide; or

a6) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope;

ii) the first MHC polypeptide; and

iii) at least one immunomodulatory polypeptide; and

b6) the second polypeptide comprises:

i) the second MHC polypeptide.

5. A T-cell modulatory multimeric polypeptide of any one of claims 1-4, wherein:

a) the first MHC polypeptide is a β2-microglobulin polypeptide; and the second MHC polypeptide is an MHC class I heavy chain polypeptide; or

b) the first MHC polypeptide is an MHC class I heavy chain polypeptide; and the second MHC polypeptide is a β2-microglobulin polypeptide.

6. A T-cell modulatory multimeric polypeptide of claim 5, wherein:

a) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the β2-microglobulin polypeptide; and

b) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) at least one immunomodulatory polypeptide;

ii) the MHC class I heavy chain polypeptide; and

iii) an Ig Fc polypeptide.

7. A T-cell modulatory multimeric polypeptide of claim 5, wherein:

a) the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the peptide epitope; and

ii) the β2-microglobulin polypeptide; and

b) the second polypeptide comprises, in order from N-terminus to C-terminus:

i) the MHC class I heavy chain polypeptide; and

ii) an Ig Fc polypeptide; and

iii) at least one immunomodulatory polypeptide

8. A T-cell modulatory multimeric polypeptide of any one of claims 1-7, wherein the at least one immunomodulatory polypeptide is selected from the group consisting of a cytokine, a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, a CD40 polypeptide, a CD70 polypeptide, and combinations thereof.

9. A T-cell modulatory multimeric polypeptide of any one of claims 1-8, wherein the at least one immunomodulatory polypeptide is an IL-2 polypeptide.

10. A T-cell modulatory multimeric polypeptide of any one of claims 1-9, wherein the multimeric polypeptide comprises at least two immunomodulatory polypeptides, and wherein at least two of the immunomodulatory polypeptides are the same, optionally wherein the 2 or more immunomodulatory polypeptides are in tandem.

11. A T-cell modulatory multimeric polypeptide of any one of claims 1-10, wherein the immunomodulatory polypeptide is a variant IL-2 polypeptide that exhibits reduced affinity to an IL-2 receptor compared to the affinity of a wild-type IL-2 polypeptide for the IL-2 receptor.

12. A T-cell modulatory multimeric polypeptide of claim 11, wherein the variant IL-2 polypeptide comprises: i) an H16A substitution and an F42A substitution; or ii) an H16T substitution and an F42A substitution.

13. A T-cell modulatory multimeric polypeptide of any one of claims 1-12, wherein the first polypeptide and the second polypeptide are covalently linked to one another, optionally wherein the covalent linkage is via a disulfide bond.

14. A T-cell modulatory multimeric polypeptide of any one of claims 1-13, wherein the first MHC polypeptide or a linker between the epitope and the first MHC polypeptide comprises an amino acid substitution to provide a first Cys residue, wherein the second MHC polypeptide comprises an amino acid substitution to provide a second Cys residue, and wherein the disulfide linkage is between the first and the second Cys residues.

15. The T-cell modulatory multimeric polypeptide of any one of claims 1-14, wherein the polypeptide comprises a disulfide bond between: i) a Cys present in a linker between the peptide epitope and the first MHC class I polypeptide, wherein the first MHC class I polypeptide is a β2M polypeptide; and ii) a Cys residue introduced via a Y84C substitution in the second MHC class I polypeptide, wherein the second MHC class I polypeptide is a MHC Class I heavy chain polypeptide.

16. The T-cell modulatory multimeric polypeptide of any one of claims 1-14, wherein the polypeptide comprises a disulfide bond between i) a Cys residue introduced into the first MHC class I polypeptide via an R12C substitution, wherein the first MHC class I polypeptide is a β2M polypeptide; and ii) a Cys residue introduced into the second MHC class I polypeptide, via an A236C substitution, wherein second MHC class I polypeptide is an MHC Class I heavy chain polypeptide.

17. The T-cell modulatory multimeric polypeptide of any one of claims 1-14, wherein the polypeptide comprises a first disulfide bond between: i) a Cys present in a linker between the peptide epitope and the first MHC class I polypeptide, wherein the first MHC class I polypeptide is a β2M polypeptide; and ii) a Cys residue introduced via a Y84C substitution in the second MHC class I polypeptide, wherein the second MHC class I polypeptide is a MHC Class I heavy chain polypeptide, and a second disulfide bond between i) a Cys residue introduced into the β2M polypeptide via an R12C substitution; and ii) a Cys residue introduced into the MHC Class I heavy chain polypeptide via an A236C substitution.

18. A T-cell modulatory multimeric polypeptide of claim 15 or claim 17, wherein the linker between the peptide epitope and the first MHC is GCGGS(G4S)n (SEQ ID NO:315), where n is 1, 2, 3, 4, 5, 6, 7, 8, or 9.

19. A T-cell modulatory multimeric polypeptide of any one of claims 1-18, wherein the peptide epitope has a length of from about 4 amino acids to about 25 amino acids.

20. A T-cell modulatory multimeric polypeptide of any one of claims 1-19, wherein the peptide epitope is other than a peptide epitope of a human papilloma virus (HPV) antigen, an alpha-feto protein (AFP) antigen, and a Wilms tumor-1 (WT1) antigen.

21. A T-cell modulatory multimeric polypeptide of any one of claims 1-20, wherein the first or the second MHC polypeptide comprises:

a) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-A*0101, HLA-A*0201, HLA-A*0201, HLA-A*1101, HLA-A*2301, HLA-A*2402, HLA-A*2407, HLA-A*3303, or HLA-A*3401 amino acid sequence depicted in FIG. 11A; or

b) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-B*0702, HLA-B*0801, HLA-B*1502, HLA-B*3802, HLA-B*4001, HLA-B*4601, or HLA-B*5301 amino acid sequence depicted in FIG. 12A; or

c) an amino acid sequence having at least 95% amino acid sequence identity to the HLA-C*0102, HLA-C*0303, HLA-C*0304, HLA-C*0401, HLA-C*0602, HLA-C*0701, HLA-C*0702, HLA-C*0801, or HLA-C*1502 depicted in FIG. 13A.

22. A T-cell modulatory multimeric polypeptide of any one of claims 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*2402 polypeptide.

23. A T-cell modulatory multimeric polypeptide of any one of claims 1-20, wherein the first MHC polypeptide is a β2M polypeptide, and wherein the second MHC polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to an HLA-A*0201 polypeptide.

24. A T-cell modulatory multimeric polypeptide of any one of claims 1-23, wherein the multimeric polypeptide comprises a first and a second heterodimer, and wherein the first and second heterodimers are covalently bound by one or more disulfide bonds between the Ig Fc polypeptides of the first and second heterodimers.

25. A nucleic acid comprising a nucleotide sequence encoding a first or second polypeptide according to any one of claims 1-24.

26. An expression vector comprising the nucleic acid of claim 25.

27. A method of selectively modulating the activity of T cell specific for a peptide epitope, the method comprising contacting the T cell with a T-cell modulatory multimeric polypeptide according to any one of claims 1-24, wherein said contacting selectively modulates the activity of the epitope-specific T cell.

28. A method of treating a patient having a cancer, the method comprising administering to the patient an effective amount of a pharmaceutical composition comprising T-cell modulatory multimeric polypeptide according to any one of claims 1-24.

29. A method of claim 28, further comprising administering one or more checkpoint inhibitors to the individual.

30. A method according to claim 29, wherein the checkpoint inhibitor is an antibody that binds to a polypeptide selected from the group consisting of CD27, CD28, CD40, CD122, CD96, CD73, CD47, OX40, GITR, CSF1R, JAK, PI3K delta, PI3K gamma, TAM, arginase, CD137, ICOS, A2AR, B7-H3, B7-H4, BTLA, CTLA-4, LAG3, TIM3, VISTA, CD96, TIGIT, CD122, PD-1, PD-L1, and PD-L2.

31. A method according to claim 30, wherein the checkpoint inhibitor is an antibody specific for PD-1, PD-L1, or CTLA4.

32. A method according to claim 29, wherein the one or more checkpoint inhibitors is selected from the group consisting of nivolumab, pembrolizumab, pidilizumab, AMP-224, MPDL3280A, MDX-1105, MEDI-4736, arelumab, ipilimumab, tremelimumab, pidilizumab, IMP321, MGA271, BMS-986016, lirilumab, urelumab, PF-05082566, IPH2101, MEDI-6469, CP-870,893, Mogamulizumab, Varlilumab, Avelumab, Galiximab, AMP-514, AUNP 12, Indoximod, NLG-919, INCB024360, KN035, and combinations thereof.

33. A method of modulating an immune response in an individual, the method comprising administering to the individual an effective amount of the T-cell modulatory multimeric polypeptide of any one of claims 1-24,

wherein said administering induces an epitope-specific T cell response and an epitope-non-specific T cell response, and

wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 2:1.

34. A method of delivering an immunomodulatory polypeptide selectively to a target T cell, the method comprising contacting a mixed population of T cells with a T-cell modulatory multimeric polypeptide of any one of claims 1-24, wherein the mixed population of T cells comprises the target T cell and non-target T cells, wherein the target T cell is specific for the epitope present within the T-cell modulatory multimeric polypeptide, and wherein said contacting delivers the one or more immunomodulatory polypeptides present within the T-cell modulatory multimeric polypeptide to the target T cell.

35. A method of detecting, in a mixed population of T cells obtained from an individual, the presence of a target T cell that binds a peptide epitope, the method comprising:

a) contacting *in vitro* the mixed population of T cells with the T-cell modulatory multimeric polypeptide of any one of claims 1-24, wherein the T-cell modulatory multimeric polypeptide comprises the peptide epitope; and

b) detecting activation and/or proliferation of T cells in response to said contacting, wherein activated and/or proliferated T cells indicates the presence of the target T cell.

FIG. 1A

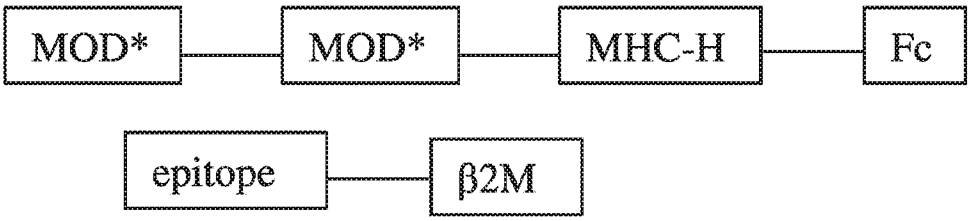


FIG. 1B

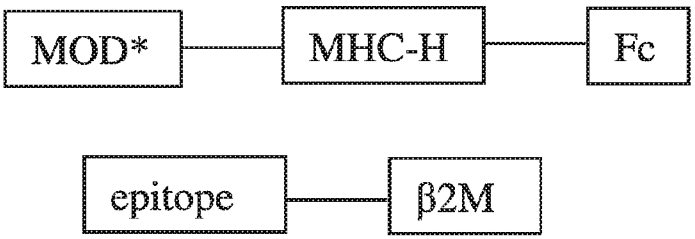


FIG. 1C

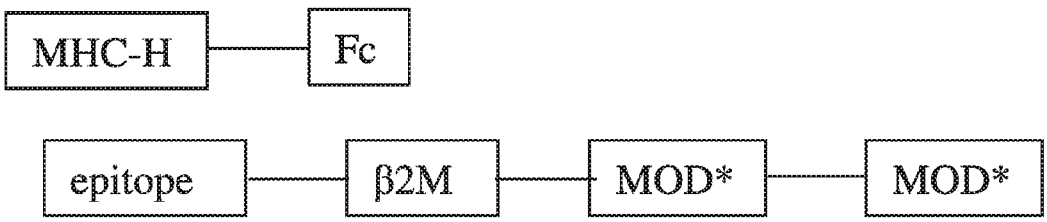


FIG. 1D

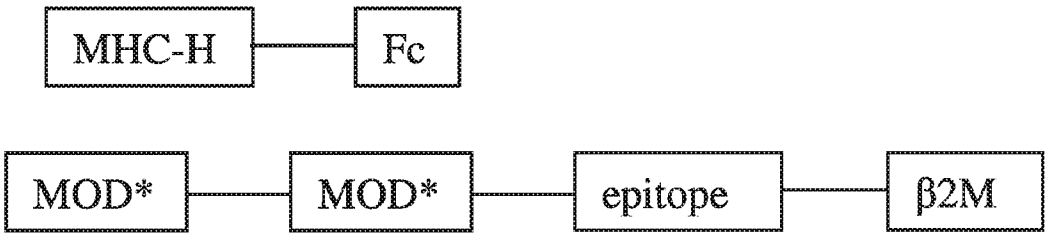


FIG. 1E

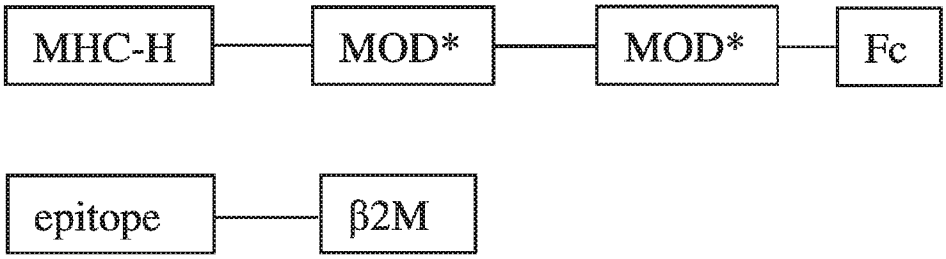


FIG. 1F

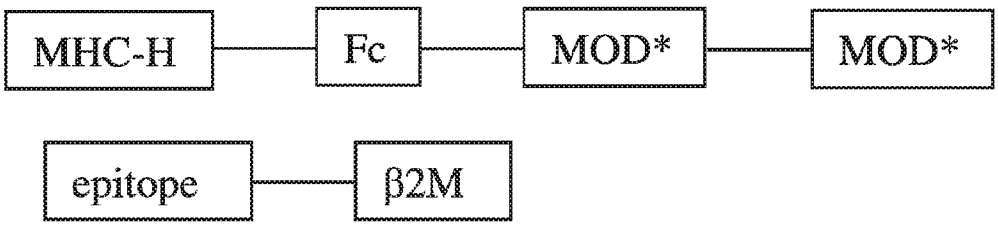


FIG. 2A

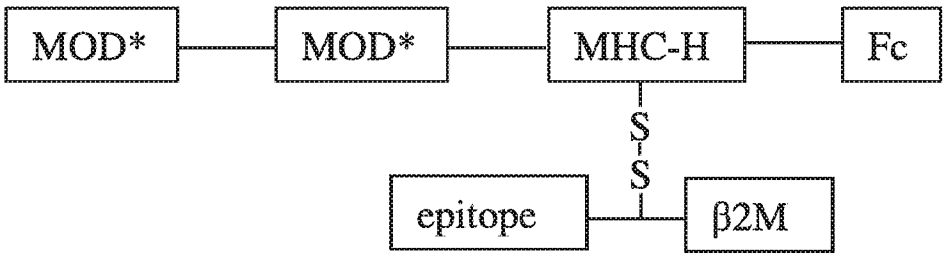


FIG. 2B

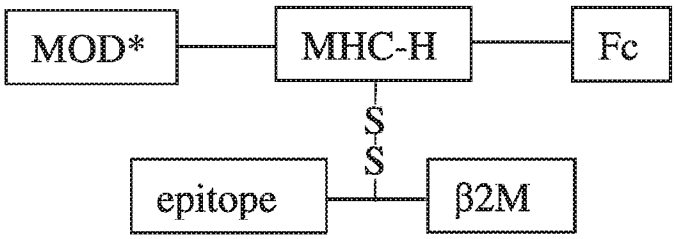


FIG. 2C

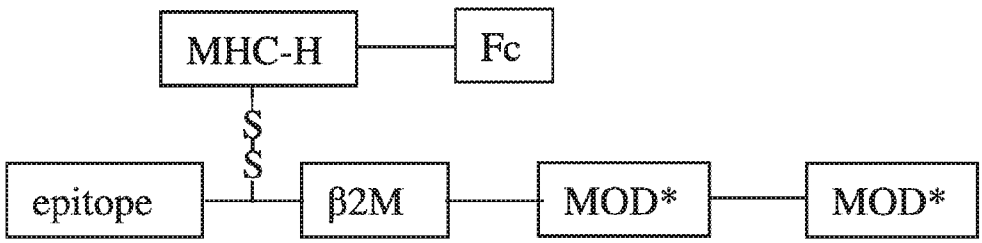


FIG. 2D

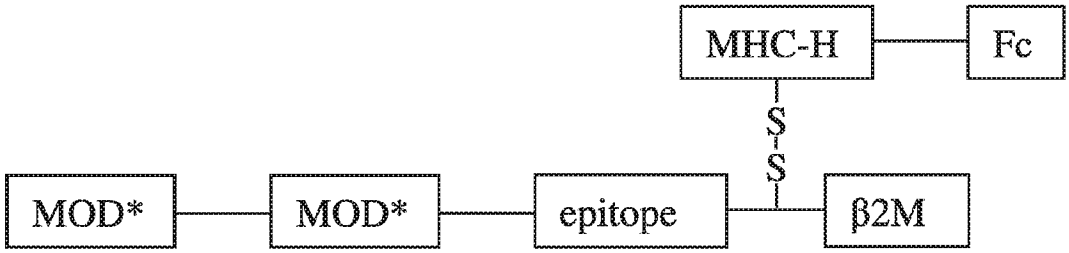


FIG. 2E

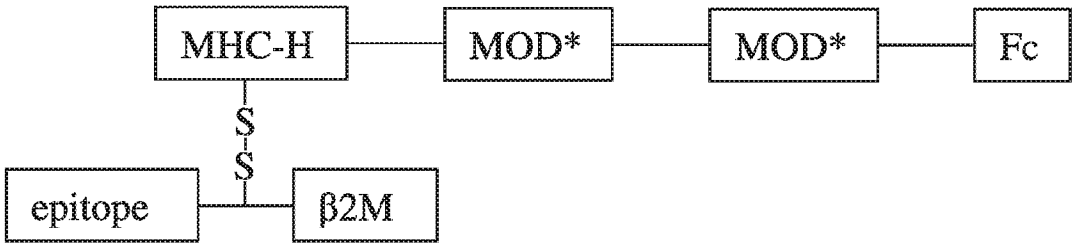


FIG. 2F

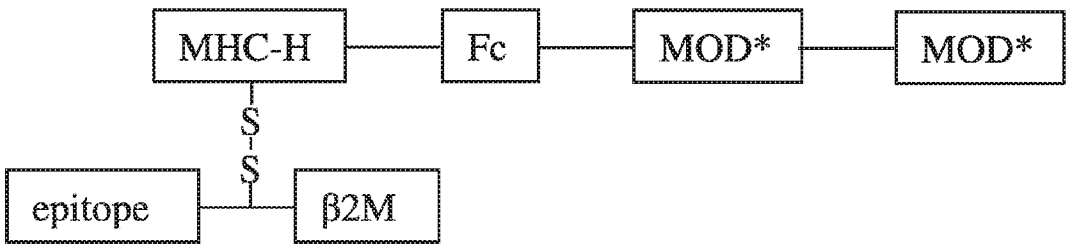


FIG. 3A

GenBank 3S7G_A
Homo sapiens **IgG1** Fc (SEQ ID NO://)
227 aa

```
  1 dkthtcppcp apellggpsv flfppkpkdt lmisrtpevt cvvvdvshed pevkfnwyvd
 61 gvevhnaktk preeqynsty rvvsvltvlh qdwlngkeyk ckvsnkalpa piektiskak
121 gqprepqvyt lppsrdeltk nqvsltclvk gfypsdiave wesngqpenn ykttppvlds
181 dgsfflyskl tvdksrwqqg nvfscsvmhe alhnhytqks lslspgk
```

GenBank AAN76044
Homo sapiens **IgG2** Fc (amino acids 99-325) (SEQ ID NO://)
227 aa

```
  1 stkgpsvfpl apcsrstses taalgclvkd yfpepvtvsw nsgaltsgvh tfpavlqssg
 61 lyslssvvtv pssnfgtqty tcnvdhkpsn tkvdktverk ccvecppcpa ppvagpsvfl
121 fppkpkdtlm isrtpevtcv vvdvshedpe vqfnwyvdgv evhnaktkpr eeqfnstfrv
181 vsvltvvhqd wlngkeykck vsnkglpapi ektisktkgq prepqvytlp psreemtknq
241 vsltclvkgf ypsdiavewe sngqpennyk ttppmldsdg sfflyskltv dksrwqqgnv
301 fscsvmheal hnhytqksls lspgk
```

GenBank AAW65947
Homo sapiens **IgG3** Fc (amino acids 19-246) (SEQ ID NO://)
238 aa

```
  1 hkpsntkvdk rvelktplgd tthtcppcpa pellggpsvf lfppkpkdtl misrtpevtc
 61 vvvdvshedp evkfnwyvdg vevhnaktkp reeqynstyr vvsvltvlhq dwlngkeykc
121 kvsnkalpap iektiskakg qprepqvytl ppsrdeltkn qvsltclvkg fypsdiavew
181 esngqpenny kttppvldsd gsfflysklt vdksrwqqgn vfscsvmhea lhnhytqksl
241 slspgk
```

FIG. 3B

GenBank AAA52770
Homo sapiens **IgD** Fc (amino acids 162-383) (SEQ ID NO://)
222 aa

```
  1 ptkapdvfpi isgcrhpkdn spvvlaclit gyhptsvtvt wymgtqsqpq rtfpeiqrrd
 61 syymtssqls tplqqwrqge ykcvvqhtas kskkeifrwp espkaqassv ptaqpqaegs
121 lakattapat trntgrggee kkkekekeeq eeretktpec pshtqplgvy lltpavqdlw
181 lrdkatftcf vvgsdlkdah ltwevagkvp tggveeglle rhsngsqsqh srltlprslw
241 nagtsvtctl nhpslppqrl malrepaaqa pvklslnlla ssdppeaasw llcevsgfsp
301 pnillmwled qrevntsgfa parpppqprs ttfwawsvlr vpappspqpa tytcvvshed
361 srtllnasrs levsyvtdhg pmk
```

GenBank 0308221A
Homo sapiens **IgM** Fc (SEQ ID NO://)
276 aa

```
  1 vtstltikzs dwlgesmftc rvdhrgltfq qnassmcvpd qdtairvfai ppsfasiflt
 61 kstkltclvt dlttybsvti swtreengav kthtnisesh pnatfsavge asicedbdws
121 gerftctvth tdlpsplkqt isrpkgvalh rpbvyllppa rzzlnlresa titclvtgfs
181 padvfvewmq rgeplspqky vtsapmpepq apgryfahsi ltvseeewnt ggtytcvvah
241 ealpnrvter tvdkstgkpt lynvslvmsd tagtcy
```

FIG. 3C

GenBank P01876

Homo sapiens **IgA** Fc (amino acids 120-353) (SEQ ID NO://)

234 aa

```
  1 asptspkvfp lslcstqpdg nvviaclvqg ffpqeplsvt wsesgqgvta rnfppsqdas
 61 gdlyttssql tlpatqclag ksvtchvkhy tnpsqdvtvp cpvpstpptp spstpptpsp
121 scchprlslh rpaledlllg seanltctlt glrdasgvtf twtpssgksa vqgpperdlc
181 gcysvssvlp gcaepwnhgk tftctaaype sktpltatls ksgntfrpev hllpppseel
241 alnelvtltc largfspkdv lvrwlqgsqe lprekyltwa srqepsqgtt tfavtsilrv
301 aaedwkkgdt fscmvgheal plaftqktid rlagkpthvn vsvvmaevdg tcy
```

GenBank 1F6A_B

Homo sapiens **IgE** Fc (amino acids 6-222) (SEQ ID NO://)

212 aa

```
  1 adpcdsnprg vsaylsrpsp fdlfirkspt itclvvdlap skgtvnltws rasgkpvnhs
 61 trkeekqrng tltvtstlpv gtrdwieget yqcrvthphl pralmrsttk tsgpraapev
121 yafatpewpg srdkrtlacl iqnfmpedis vqwlhnevql pdarhsttqp rktkgsgffv
181 fsrlevtrae weqkdeficr avheaaspsq tvqravsvnp gk
```

GenBank P01861

Homo sapiens **IgG4** Fc (amino acids 100-327) (SEQ ID NO://)

228 aa

```
  1 astkgpsvfp lapcsrstse staalgclvk dyfpepvtvs wnsgaltsgv htfpavlqss
 61 glyslssvvt vpssslgtkt ytcnvdhkps ntkvdkrves kygppcpscp apeflggpsv
121 flfppkpkdt lmisrtpevt cvvvdvsqed pevqfnwyvd gvevhnaktk preeqfnsty
181 rvvsvltvlh qdwlngkeyk ckvsnkglps siektiskak gqprepqvyt lppsqeemtk
241 nqvsltclvk gfypsdiave wesngqpenn ykttppvlds dgsfflysrl tvdksrwqeg
301 nvfscsvmhe alhnhytqks lslslgk
```

FIG. 3D

WT Human IgG1 Fc Sequence: (SEQ ID NO://)
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 3E

Human IgG1 Fc Mutant: L234F/L235E/P331S (Triple Mutant "TM") (SEQ ID NO://)
DKTHTCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 3F

Human IgG1 Fc Mutant: N297A (SEQ ID NO://)
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 3G

Human IgG1 Fc Mutant: L234A/L235A ("LALA") (SEQ ID NO://)
DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST
YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE
WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Residue numbered according to EU index (Kabat Numbering)

FIG. 4

```
NP_004039.1     msrsvalavlallslsgleaiqrtpkiqvysrhpaengksnflncyvsgfhpsdievdll 60
NP_001009066.1  msrsvalavlallslsgleaiqrtpkiqvysrhpaengksnflncyvsgfhpsdievdll 60
NP_001040602.1  msrsvalavlallslsgleaiqrtpkiqvysrhppengkpnflncyvsgfhpsdievdll 60
NP_776318.1     marfvalvllglllslsgldaiqrppkiqvysrhppedgkpnylncyvygfhppqieidll 60
NP_033865.2     marsvtlvflvlvsltglyaiqktpqiqvysrhppengkpnilncyvtqfhpphieiqml 60
                *:* *:*:..* *:**:** ***: *:********* *:** * ***** *** .**:::*

NP_004039.1     kngeriekvehsdlsfskdwsfyllyyteftptekdeyacrvnhvtlsqpkivkwdrdm 119 (SEQ ID NO://)
NP_001009066.1  kngeriekvehsdlsfskdwsfyllyyteftptekdeyacrvnhvtlsqpkivkwdrdm 119 (SEQ ID NO://)
NP_001040602.1  kngekmgkvehsdlsfskdwsfyllyyteftpnekdeyacrvnhvtlsgprtvkwdrdm 119 (SEQ ID NO://)
NP_776318.1     kngekik-seqsdlsfskdwsfyllshaeftpnskdqyscrvkhvtleqprivkwdrdl 118 (SEQ ID NO://)
NP033865        kngkkipkvemsdmsfskdwsfyilahteftptetdtyacrvkhasmaepkttvywdrdm 119 (SEQ ID NO://)
                *******   * **:**********:* ::***** ...* *:****:*.::  *: * *****:
```

FIG. 5A

Homo sapiens HLA-A

5A.1 HLA-A*01:01:01:01 NCBI (National Center for Biotechnology Information) Accession NP_001229687.1

(SEQ ID NO://)

```
  1 MAVMAPRTLL LLLSGALALT QTWAGSHSMR YFFTSVSRPG RGEPRFIAVG YVDDTQFVRF
 61 DSDAASQKME PRAPWIEQEG PEYWDQETRN MKAHSQTDRA NLGTLRGYYN QSEDGSHTIQ
121 IMYGCDVGPD GRFLRGYRQD AYDGKDYIAL NEDLRSWTAA DMAAQITKRK WEAVHAAEQR
181 RVYLEGRCVD GLRRYLENGK ETLQRTDPPK THMTHHPISD HEATLRCWAL GFYPAEITLT
241 WQRDGEDQTQ DTELVETRPA GDGTFQKWAA VVVPSGEEQR YTCHVQHEGL PKPLTLRWEL
301 SSQPTIPIVG IIAGLVLLGA VITGAVVAAV MWRRKSSDRK GGSYTQAASS DSAQGSDVSL
361 TACKV
```

5A.2 HLA-A*1101 NCBI Accession P13746.1 (SEQ ID NO://)

```
  1 MAVMAPRTLL LLLSGALALT QTWAGSHSMR YFYTSVSRPG RGEPRFIAVG YVDDTQFVRF
 61 DSDAASQRME PRAPWIEQEG PEYWDQETRN VKAQSQTDRV DLGTLRGYYN QSEDGSHTIQ
121 IMYGCDVGPD GRFLRGYRQD AYDGKDYIAL NEDLRSWTAA DMAAQITKRK WEAAHAAEQQ
181 RAYLEGRCVE WLRRYLENGK ETLQRTDPPK THMTHHPISD HEATLRCWAL GFYPAEITLT
241 WQRDGEDQTQ DTELVETRPA GDGTFQKWAA VVVPSGEEQR YTCHVQHEGL PKPLTLRWEL
301 SSQPTIPIVG IIAGLVLLGA VITGAVVAAV MWRRKSSDRK GGSYTQAASS DSAQGSDVSL
361 TACKV
```

5A.3 HLA-A*2402 NCBI Accession P05534.2 (SEQ ID NO://)

```
  1 MAVMAPRTLV LLLSGALALT QTWAGSHSMR YFSTSVSRPG RGEPRFIAVG YVDDTQFVRF
 61 DSDAASQRME PRAPWIEQEG PEYWDEETGK VKAHSQTDRE NLRIALRYYN QSEAGSHTLQ
121 MMFGCDVGSD GRFLRGYHQY AYDGKDYIAL KEDLRSWTAA DMAAQITKRK WEAAHVAEQQ
181 RAYLEGTCVD GLRRYLENGK ETLQRTDPPK THMTHHPISD HEATLRCWAL GFYPAEITLT
241 WQRDGEDQTQ DTELVETRPA GDGTFQKWAA VVVPSGEEQR YTCHVQHEGL PKPLTLRWEP
301 SSQPTVPIVG IIAGLVLLGA VITGAVVAAV MWRRNSSDRK GGSYSQAASS DSAQGSDVSL
361 TACKV
```

5A.4 HLA-A*3303 NCBI Accession AAA79865.1 (SEQ ID NO://)

```
  1 MAVMAPRTLL LLLLGALALT QTWAGSHSMR YFTTSVSRPG RGEPRFIAVG YVDDTQFVRF
 61 DSDAASQRME PRAPWIEQEG PEYWDRNTRN VKAHSQIDRV DLGTLRGYYN QSEAGSHTIQ
121 MMYGCDVGSD GRFLRGYQQD AYDGKDYIAL NEDLRSWTAA DMAAQITQRK WEAARVAEQL
181 RAYLEGTCVE WLRRYLENGK ETLQRTDPPK THMTHHAVSD HEATLRCWAL SFYPAEITLT
241 WQRDGEDQTQ DTELVETRPA GDGTFQKWAS VVVPSGQEQR YTCHVQHEGL PKPLTLRWEP
301 SSQPTIPIVG IIAGLVLFGA VFAGAVVAAV RWRRKSSDRK GGSYSQAASS DSAQGSDMSL
361 TACKV
```

FIG. 5B

Homo sapiens HLA-B*07:02:01 HLA-B GenBank Accession NP_005505.2
(SEQ ID NO://)

```
  1 mlvmaprtvl lllsaalalt etwagshsmr yfytsvsrpg rgeprfisvg yvddtqfvrf
 61 dsdaaspree prapwieqeg peywdrntqi ykaqaqtdre slrnlrgyyn qseagshtlq
121 smygcdvgpd grllrghdqy aydgkdyial nedlrswtaa dtaaqitqrk weaareaeqr
181 raylegecve wlrrylengk dkleradppk thvthhpisd heatlrcwal gfypaeitlt
241 wqrdgedqtq dtelvetrpa gdrtfqkwaa vvvpsgeeqr ytchvqhegl pkpltlrwep
301 ssqstvpivg ivaglavlav vvigavvaav mcrrkssggk ggsysqaacs dsaqgsdvsl
361 ta
```

FIG. 5C

Homo sapiens HLA-C
HLA-C GenBank Accession NP_001229971.1,
w (SEQ ID NO://)

```
  1 mrvmaprall lllsgglalt etwacshsmr yfdtavsrpg rgeprfisvg yvddtqfvrf
 61 dsdaasprge prapwveqeg peywdretqn ykrqaqadrv slrnlrgyyn qsedgshtlq
121 rmygcdlgpd grllrgydqs aydgkdyial nedlrswtaa dtaaqitqrk leaaraaeql
181 raylegtcve wlrrylengk etlqraeppk thvthhplsd heatlrcwal gfypaeitlt
241 wqrdgedqtq dtelvetrpa gdgtfqkwaa vvvpsgqeqr ytchmqhegl qepltlswep
301 ssqptipimg ivaglavlvv lavlgavvta mmcrrkssgg kggscsqaac snsaqgsdes
361 litck
```

FIG. 6

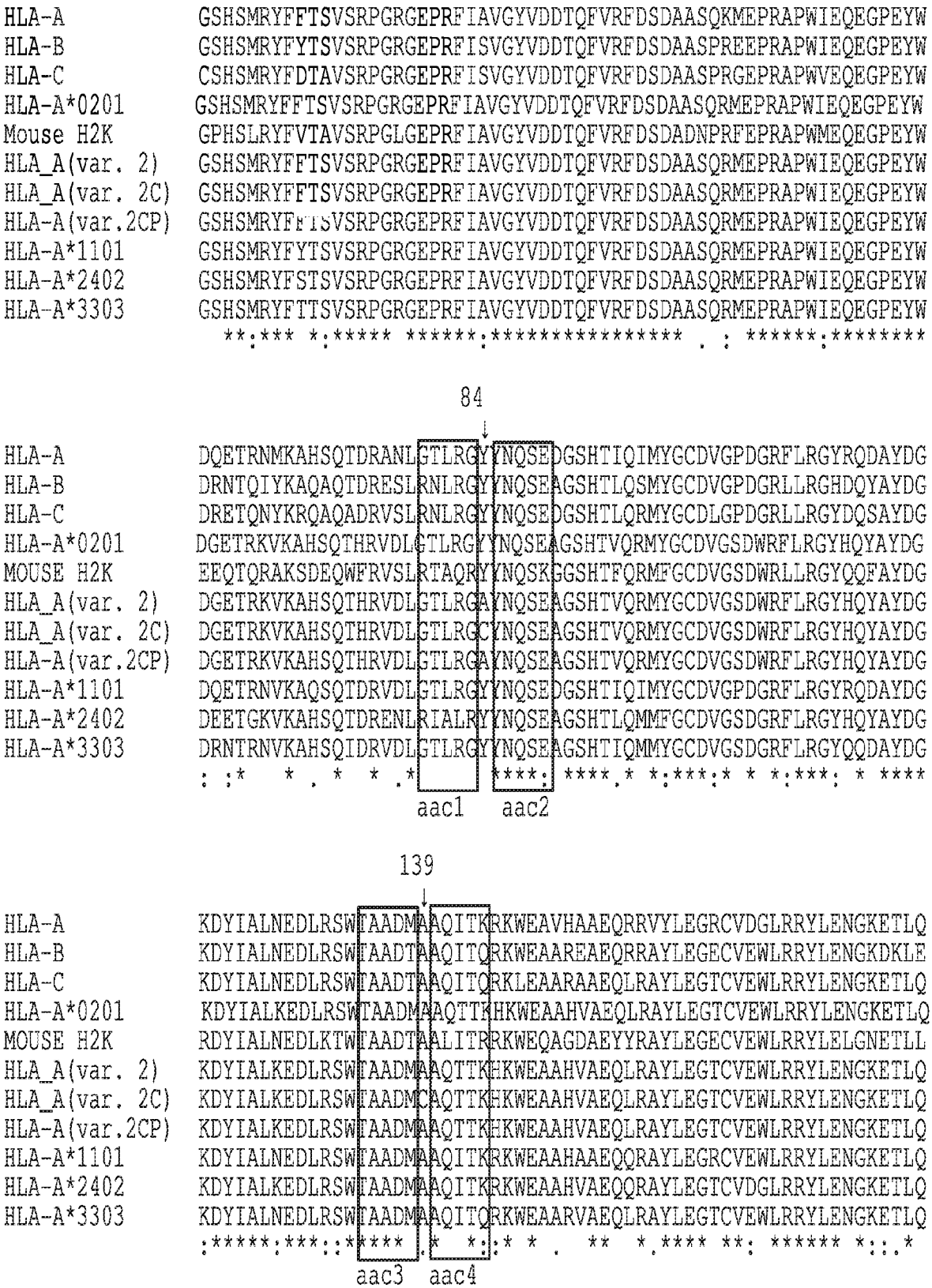
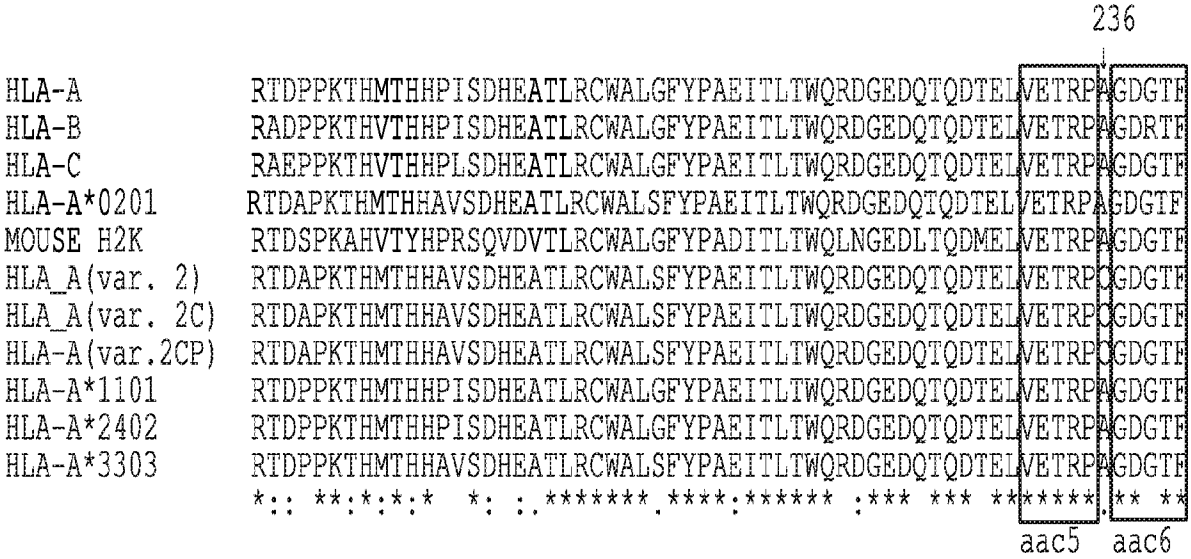

HLA-A GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQKMEPRAPWIEQEGPEYW
HLA-B GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYW
HLA-C CSHSMRYFDTAVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQEGPEYW
HLA-A*0201 GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
Mouse H2K GPHSLRYFVTAVSRPGLGEPRFIAVGYVDDTQFVRFDSDADNPRFEPRAPWMEQEGPEYW
HLA_A(var. 2) GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
HLA_A(var. 2C) GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
HLA-A(var.2CP) GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
HLA-A*1101 GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
HLA-A*2402 GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
HLA-A*3303 GSHSMRYFTTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW
84
HLA-A DQETRNMKAHSQTDRANLGTLRGYYNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDG
HLA-B DRNTQIYKAQAQTDRESLRNLRGYYNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDG
HLA-C DRETQNYKRQAQADRVSLRNLRGYYNQSEDGSHTLQRMYGCDLGPDGRLLRGYDQSAYDG
HLA-A*0201 DGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDG
MOUSE H2K EEQTQRAKSDEQWFRVSLRTAQRYYNQSKGGSHTFQRMFGCDVGSDWRLLRGYQQFAYDG
HLA_A(var. 2) DGETRKVKAHSQTHRVDLGTLRGAYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDG
HLA_A(var. 2C) DGETRKVKAHSQTHRVDLGTLRGCYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDG
HLA-A(var.2CP) DGETRKVKAHSQTHRVDLGTLRGAYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDG
HLA-A*1101 DQETRNVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDG
HLA-A*2402 DEETGKVKAHSQTDRENLRIALRYYNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDG
HLA-A*3303 DRNTRNVKAHSQIDRVDLGTLRGYYNQSEAGSHTIQMMYGCDVGSDGRFLRGYQQDAYDG
aac1
aac2
139
HLA-A KDYIALNEDLRSWTAADMAAQITKRKWEAVHAAEQRRVYLEGRCVDGLRRYLENGKETLQ
HLA-B KDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLE
HLA-C KDYIALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A*0201 KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQ
MOUSE H2K RDYIALNEDLKTWTAADTAALITRRKWEQAGDAEYYRAYLEGECVEWLRRYLELGNETLL
HLA_A(var. 2) KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQ
HLA_A(var. 2C) KDYIALKEDLRSWTAADMCAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A(var.2CP) KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A*1101 KDYIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAYLEGRCVEWLRRYLENGKETLQ
HLA-A*2402 KDYIALKEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQ
HLA-A*3303 KDYIALNEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVEWLRRYLENGKETLQ
aac3
aac4

FIG. 6 (Cont.)



HLA-A QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:)
HLA-B QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:)
HLA-C QKWAAVVVPSGQEQRYTCHMQHEGLQEPLTLSWE (SEQ ID NO:)
HLA-A*0201 QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:)
MOUSE H2K QKWAAVVVPLGKEQNYTCHVHHKGLPEPLTLRW (SEQ ID NO:)
HLA_A(var. 2) QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:)
HLA_A(var. 2C) QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE (SEQ ID NO:)
HLA-A(var.2CP) QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:)
HLA-A*1101 QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWEL (SEQ ID NO:)
HLA-A*2402 QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:)
HLA-A*3303 QKWASVVVPSGQEQRYTCHVQHEGLPKPLTLRWEP (SEQ ID NO:)

FIG. 7A

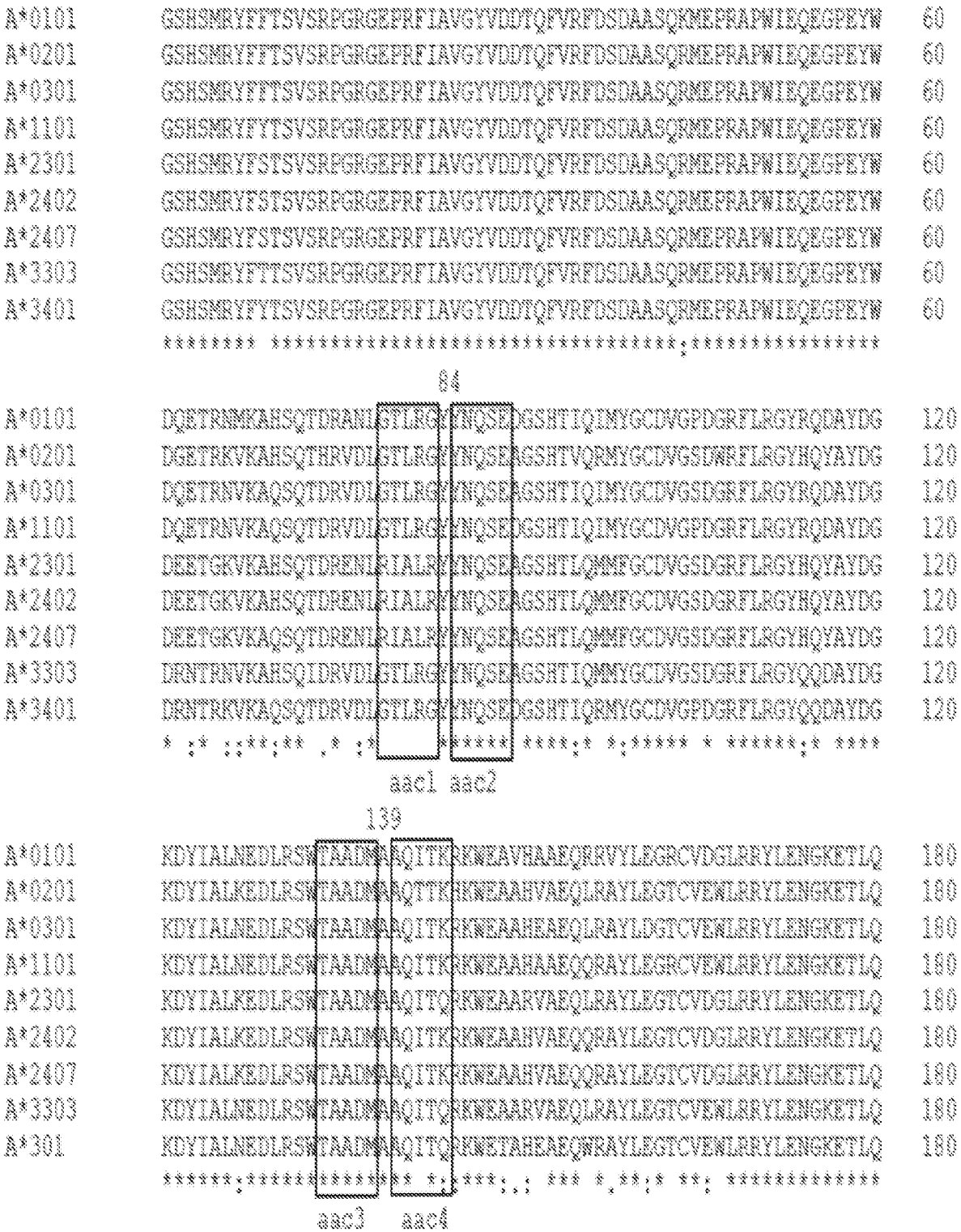

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A*0301 GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*1101 GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*2301 GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*2402 GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*2407 GSHSMRYFSTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*3303 GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
A*3401 GSHSMRYFYTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQEGPEYW 60
84
A*0101 DQETRNMKAHSQTDRANLGTLRGYYNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDG 120
A*0201 DGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDWRFLRGYHQYAYDG 120
A*0301 DQETRNVKAQSQTDRVDLGTLRGYYNQSEAGSHTIQIMYGCDVGSDGRFLRGYRQDAYDG 120
A*1101 DQETRNVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQIMYGCDVGPDGRFLRGYRQDAYDG 120
A*2301 DEETGKVKAHSQTDRENLRIALRYYNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDG 120
A*2402 DEETGKVKAHSQTDRENLRIALRYYNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDG 120
A*2407 DEETGKVKAQSQTDRENLRIALRYYNQSEAGSHTLQMMFGCDVGSDGRFLRGYHQYAYDG 120
A*3303 DRNTRNVKAHSQIDRVDLGTLRGYYNQSEAGSHTIQMMYGCDVGSDGRFLRGYQQDAYDG 120
A*3401 DRNTRKVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQRMYGCDVGPDGRFLRGYQQDAYDG 120
aac1 aac2
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A*0201 KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRAYLEGTCVEWLRRYLENGKETLQ 180
A*0301 KDYIALNEDLRSWTAADMAAQITKRKWEAAHEAEQLRAYLDGTCVEWLRRYLENGKETLQ 180
A*1101 KDYIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAYLEGRCVEWLRRYLENGKETLQ 180
A*2301 KDYIALKEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVDGLRRYLENGKETLQ 180
A*2402 KDYIALKEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQ 180
A*2407 KDYIALKEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYLEGTCVDGLRRYLENGKETLQ 180
A*3303 KDYIALNEDLRSWTAADMAAQITQRKWEAARVAEQLRAYLEGTCVEWLRRYLENGKETLQ 180
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aac3 aac4

FIG. 7A (Cont.)

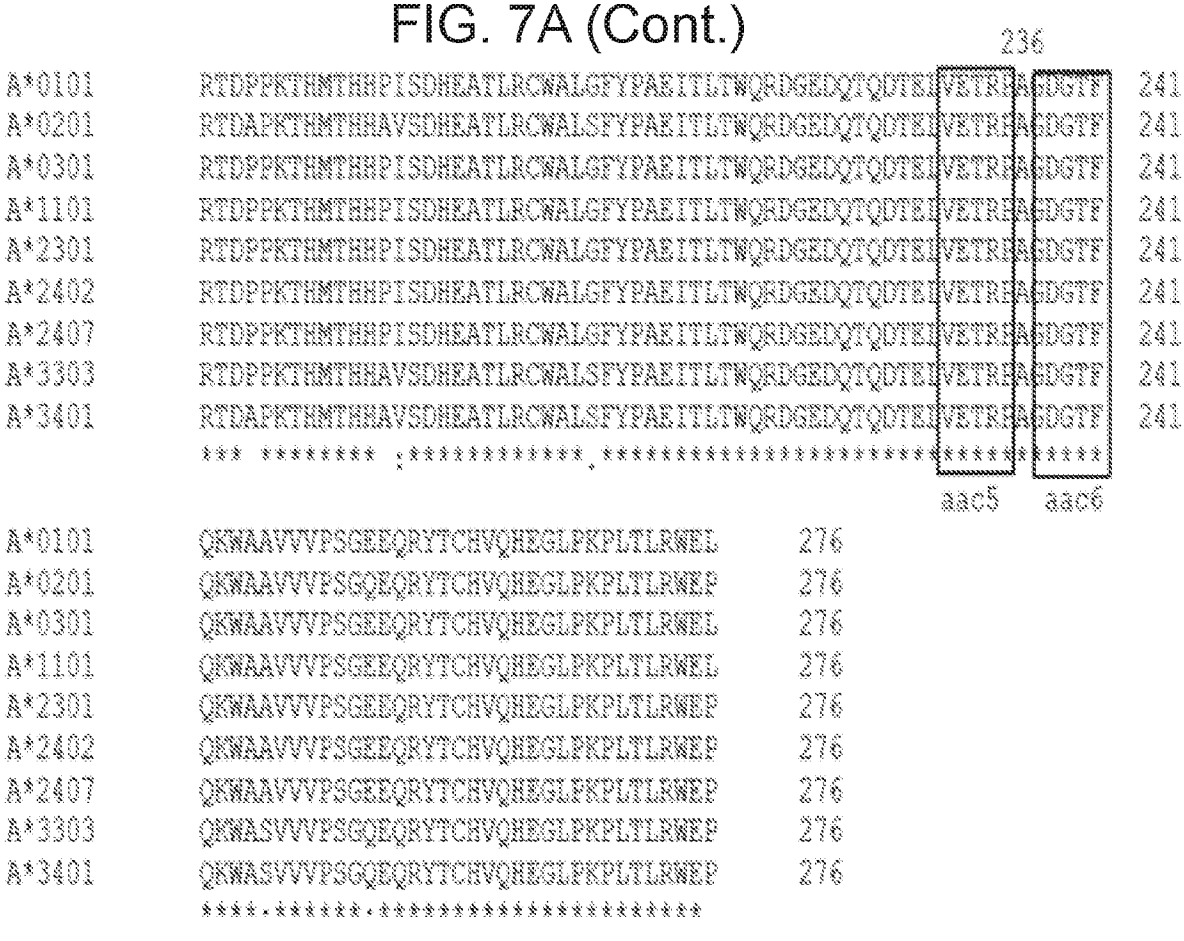


FIG. 7B

GSHSMRYF**X1**TSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQ**X2**MEPRAPWIEQEGPEYWD**X3X4**T**X5X6X7**KA**X8**SQ**X9X10**R**X11X12**L**X13X14X15X16X17Y**YNQSE**X18**GSHT**X19**Q**X20**M**X21**GCDVG**X22**D**X23**RFLRGY**X24**Q**X25**AYDGKDYIAL**X26**EDLRSWTAADM**A**AQ**X27**T**X28**7**X29**KWE**X30X31X32**EAEQ**X33**R**X34**YL**X35**G**X36**CV**X37X38**LRRYLENGKETLQRTD**X39**PK THMTHH**X40X41**SDHEATLRCWAL**X42**FYPAEITLTWQRDGEDQTQDTELVETRP**A**GDGTFQKW A**X43**VVVPSG**X44**EQRYTCHVQHEGLPKPLTLRWE**X45**

X1 is F, Y, S, or T; X2 is K or R; X3 is Q, G, E, or R; X4 is N or E; X5 is R or G; X6 is N or K; X7 is M or V; X8 is H or Q; X9 is T or I; X10 is D or H; X11 is A, V, or E; X12 is N or D; X13 is G or R; X14 is T or I; X15 is L or A; X16 is R or L; X17 is G or R; X18 is A or D; X19 is I, L, or V; X20 is I, R or M; X21 is F or Y; X22 is S or P; X23 is W or G; X24 is R, H, or Q; X25 is D or Y; X26 is N or K; X27 is T or I; X28 is K or Q; X29 is R or H; X30 is A or T; X31 is A or V; X32 is H or R; X33 is R, L, Q, or W; X34 is V or A; X35 is D or E; X36 is R or T; X37 is D or E; X38 is W or G; X39 is P or A; X40 is P or A; X41is V or I; X42 is S or G; X43 is A or S; X44 is Q or E; and X45 is P or L.

FIG. 8A

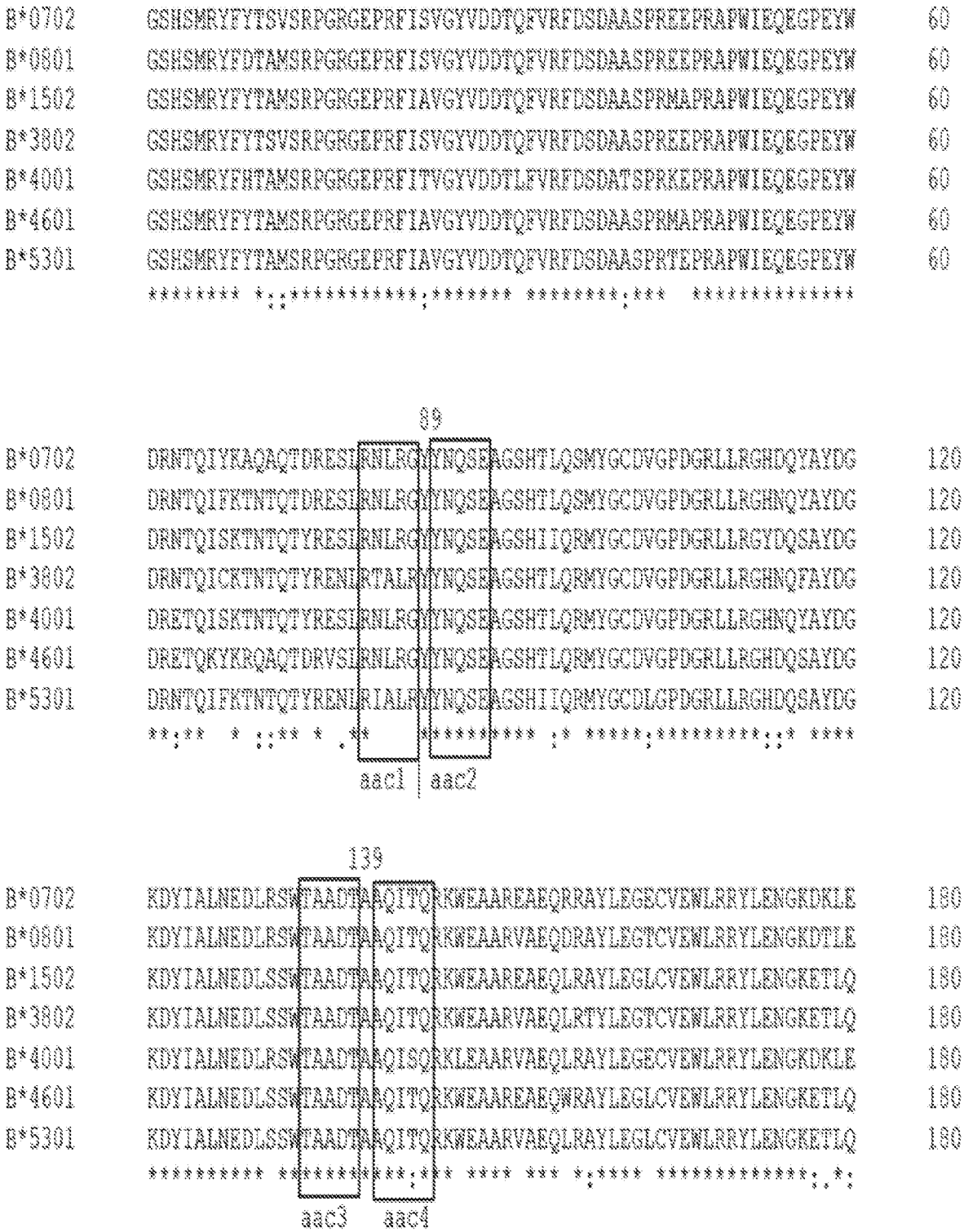

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B*0801 GSHSMRYFDTAMSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYW 60
B*1502 GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRMAPRAPWIEQEGPEYW 60
B*3802 GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQEGPEYW 60
B*4001 GSHSMRYFHTAMSRPGRGEPRFITVGYVDDTLFVRFDSDATSPRKEPRAPWIEQEGPEYW 60
B*4601 GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRMAPRAPWIEQEGPEYW 60
B*5301 GSHSMRYFYTAMSRPGRGEPRFIAVGYVDDTQFVRFDSDAASPRTEPRAPWIEQEGPEYW 60
89
B*0702 DRNTQIYKAQAQTDRESLRNLRGYYNQSEAGSHTLQSMYGCDVGPDGRLLRGHDQYAYDG 120
B*0801 DRNTQIFKTNTQTDRESLRNLRGYYNQSEAGSHTLQSMYGCDVGPDGRLLRGHNQYAYDG 120
B*1502 DRNTQISKTNTQTYRESLRNLRGYYNQSEAGSHIIQRMYGCDVGPDGRLLRGYDQSAYDG 120
B*3802 DRNTQICKTNTQTYRENLRTALRYYNQSEAGSHTLQRMYGCDVGPDGRLLRGHNQFAYDG 120
B*4001 DRETQISKTNTQTYRESLRNLRGYYNQSEAGSHTLQRMYGCDVGPDGRLLRGHNQYAYDG 120
B*4601 DRETQKYKRQAQTDRVSLRNLRGYYNQSEAGSHTLQRMYGCDVGPDGRLLRGHDQSAYDG 120
B*5301 DRNTQIFKTNTQTYRENLRIALRYYNQSEAGSHIIQRMYGCDLGPDGRLLRGHDQSAYDG 120
aac1
aac2
139
B*0702 KDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLEGECVEWLRRYLENGKDKLE 180
B*0801 KDYIALNEDLRSWTAADTAAQITQRKWEAARVAEQDRAYLEGTCVEWLRRYLENGKDTLE 180
B*1502 KDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQLRAYLEGLCVEWLRRYLENGKETLQ 180
B*3802 KDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRTYLEGTCVEWLRRYLENGKETLQ 180
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B*4601 KDYIALNEDLSSWTAADTAAQITQRKWEAAREAEQWRAYLEGLCVEWLRRYLENGKETLQ 180
B*5301 KDYIALNEDLSSWTAADTAAQITQRKWEAARVAEQLRAYLEGLCVEWLRRYLENGKETLQ 180
aac3
aac4

FIG. 8A (Cont.)

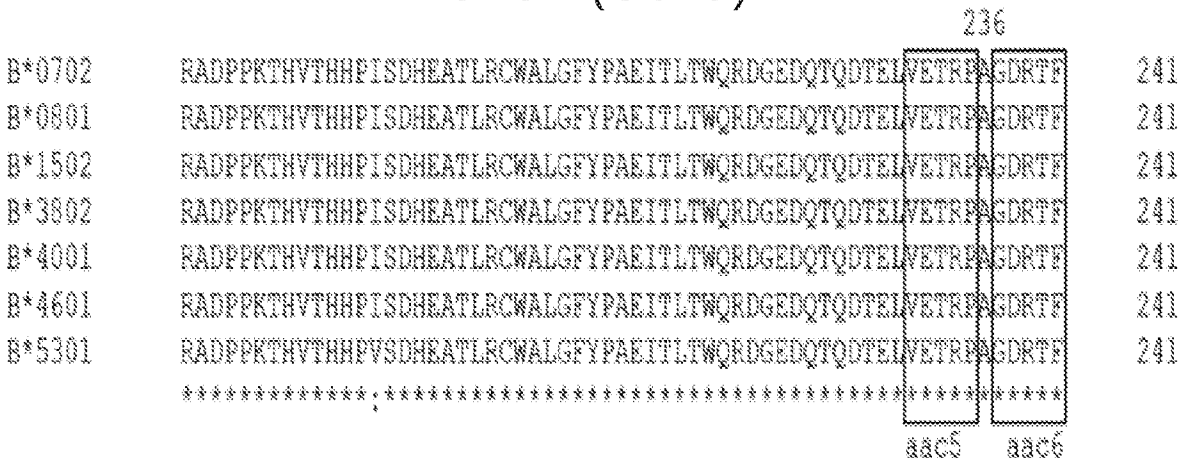


FIG. 8B

GSHSMRYF**X1**T**X2X3**SRPGRGEPRFI**X4**VGYVDDT**X5**FVRFDSDA**X6**SPR**X7X8**PRAPWIEQEG PEYWDR**X9**TQ**X10X11**KT**X12X13**TQ**X14**Y**X15X16**NL**X17X18X19X20**YYNQSEAGSH**X21X 22QX23**MYGCDLGPDGRLLRGHDQSAYDGKDYIALNEDL**X24**SWTAADTAAQI**X25**QRK**X26**EA ARX27AEQ**X28**R**X29**YLEG**X30**CVEWLRRYLENGK**X31X32**L**X33**RADPPKTHVTHHP**X34**SDH EATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDRTFQKWAAVVVPSGEEQRYTCHV QHEGLPKPLTLRWEP

X1 is H, Y, or D; X2 is A or S; X3 is M or V; X4 is A, S, or T; X5 is Q or L; X6 is A or T; X7 is E, M K, or T; X8 is A or T; X9 is E or N; X10 is I or K; X11 is Y, F, S, or C; X12 is N or Q; X13 is A or T; X14 is D or Y; X15 is E or V; X16 is S or N; X17 is T, N, or I; X18 is A or L; X19 is L, or R; X20 is R or G; X21 is T or I; X22 is L or I; X23 is R or S; X24 is R or S; X25 is S or T; X26 is L or W; X27 is E OR V; X28 is R, D, L or W; X29 is A or T; X30 is L, E or T; X31 is E or D; X32 is K or T; X33 is E or Q; and X34 is I or V.

FIG. 9A



FIG. 9A (Cont.)

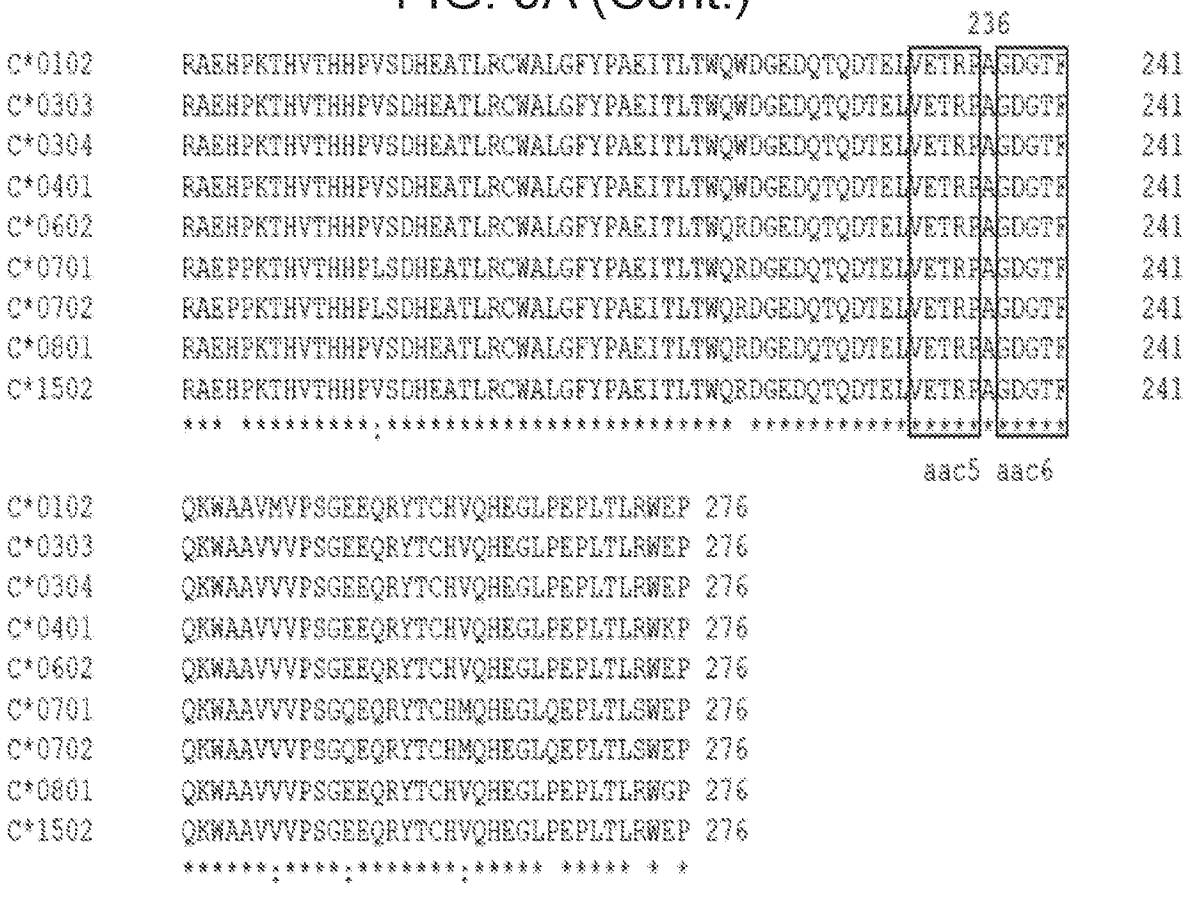


FIG. 9B

X1SHSM**X2**YF**X3**TAVS**X4**PGRGEP**X5**FI**X6**VGYVDDTQFV**X7**FDSDAASPRGEPR**X8**PWVEQEG
PEYWDRETQ**X9**YKRQAQ**X10**DRV**X11**LR**X12**LRGYYNQSE**X13X14**SH**X15X16**Q**X17**M**X18**GC
D**X19**GPDGRLLRG**X20X21**Q**X22**AYDGKDYIALNEDLRSWTAADTAAQITQRK**X23**EAAR**X24**A
EQ**X25**RAYLEG**X26**CVEWLRRYL**X27**NGK**X28**TLQRAE**X29**PKTHVTHHP**X30**SDHEATLRCWA
LGFYPAEITLTWQ**X31**DGEDQTQDTELVETRPAGDGTFQKWAAV**X32**VPS**GX33**EQRYTCH**X34**
QHEGL**X35**EPLTL**X36**W**X37**P

X1 is C or G; X2 is R or K; X3 is F, Y, S, or D; X4 is R or W; X5 is H or R; X6 is A or S; X7 is Q or R; X8 is A or E; X9 is N or K;X10 is T or A; X11 is S or N; X12 is N or K; X13 is A or D; X14 is G or R; X15 is T or I; X16 is L or I; X17 is W or R; X18 is C, Y, F, or S; X19 is L, or V; X20 is Y or H; X21 is D or N; X22 is Y, F, S, or L; X23 is L or W; X24 is E, A, Or T; X25 is R, L, or W; X26 is L or T; X27 is E OR K; X28 is E or K; X29 is H or P; X30 is R or V; X31 is W or R; X32 is V or M; X33 is E or Q; X34 is M or V; X35 is P or Q; X36 is R or S; and X37 is P or G.

FIG. 10

HLA-E

GSHSLKYFHT SVSRPGRGEP RFISVGYVDD TQFVRFDNDA ASPRMVPRAP
WMEQEGSEYW DRETRSARDT AQIFRVNLRT LRGYYNQSX1A GSHTLQWMHG
CELGPDX2RFL RGYEQFAYDG KDYLTLNEDL RSWTAVDTAA QISEQKSNDA
SEAEHQX3X4YL EDTCVEWLHK YLEKGKETLL HLEPPKTHVT HHPISDHEAT
LRCWALGFYP AEITLTWQQD GEGHTQDTEL VETRPAGDGT FQKWAAVVVP
SGEEX5RYTCH VQHEGLX6EPV TLRWKPASQP TIPI

X1= K or E; X2= R or G; X3= R or G; X4= A or V; X5= Q or P; and X6= P or S

Encompasses: HLA-E*0101 (HLA-E*01:01:01:01); HLA-E*01:03(HLA-E*01:03:01:01); HLA-E*01:04; HLA-E*01:05; HLA-E*01:06; HLA-E*01:07; HLA-E*01:09; HLA-E*01:10

HLA-F

GSHSLRX1FST AVSRPGRGEP RYIAVEYVDD TQFLRFDSDA AIPRMEPREX2
WVEQEGPQYW EWTTGYAKAN AQTDRVALRN LLRRYNQSEA GSHTLQGMNG
CDMGPDGRLL RGYHQHAYDG KDYISLNEDL RSWTAADTVA QITQRFYEAE
EYAEEFRTYL EGECLELLRR YLENGKETLQ RADPPKAHVA HHPISDHEAT
LRCWALGFYP AEITLTWQRD GEEQTQDTEL VETRPAGDGT FQKWAAVVVP
X3GEEQRYTCH VQHEGLPQPL ILRWEQSX4QP TIPI

X1= Y or F; X2= P or Q; X3= S or P; and X4= P or L

Encompasses: HLA-F*0101 (HLA-F*01:01:01:01); HLA-F*01:02; HLA-F*01:03(HLA-F*01:03:01:01); HLA-F*01:04; HLA-F*01:05; HLA-F*01:06;

HLA-G

GSHSMRYFSA AVX1RPGRGEP RFIAMGX2VDD X3QFX4RFDSDS ACPRMEPRAP
WVEX5EGPEYW EEETRNTKAH AQTDRMNLQT X6RGYYNQSEA SSHTLQWMIX7
CDLX8X9DGRLX10 RGYEQYAYDG KDYLALNEDL RSWTAADTAA QISKRKCEAA
NVAEQRRAX11L EGTCVEWLX12R X13LENGKEX14LQ RADPX15KTHVT HHPVFDYEAT
LRCWALGFYP AEIILTWQX16D GEDQTQDVEL VETRPAGDGT FQKWAAVVVP
SGEEQRYX17CH VQHEGLPEPL MLRWX18QSSLP TIPI

X1= S or F; X2= Y or H; X3= T, S, or M; X4= L or V; X5= Q or R; X6= P or L; X7= G or D; X8= G or V; X9= S or C; X10= L or I; X11= Y or H; X12= H or R; X13= Y or H; X14= M or T; X15= P or A; X16= R, W, or Q; X17= T or M; X18= K or E;

Encompasses: HLA-G*0101 (HLA-G*01:01:01:01); HLA-G*01:02; HLA-G*01:03(HLA-G*01:03:01:01); HLA-G*01:04 (HLA-G*01:04:01:01); HLA-G*01:06; HLA-G*01:07; HLA-G*01:08; HLA-G*01:09: HLA-G*01:10; HLA-G*01:10; HLA-G*01:11; HLA-G*01:12; HLA-G*01:14; HLA-G*01:15; HLA-G*01:16; HLA-G*01:17; HLA-G*01:18: HLA-G*01:19; HLA-G*01:20; HLA-G*01:22

FIG. 11

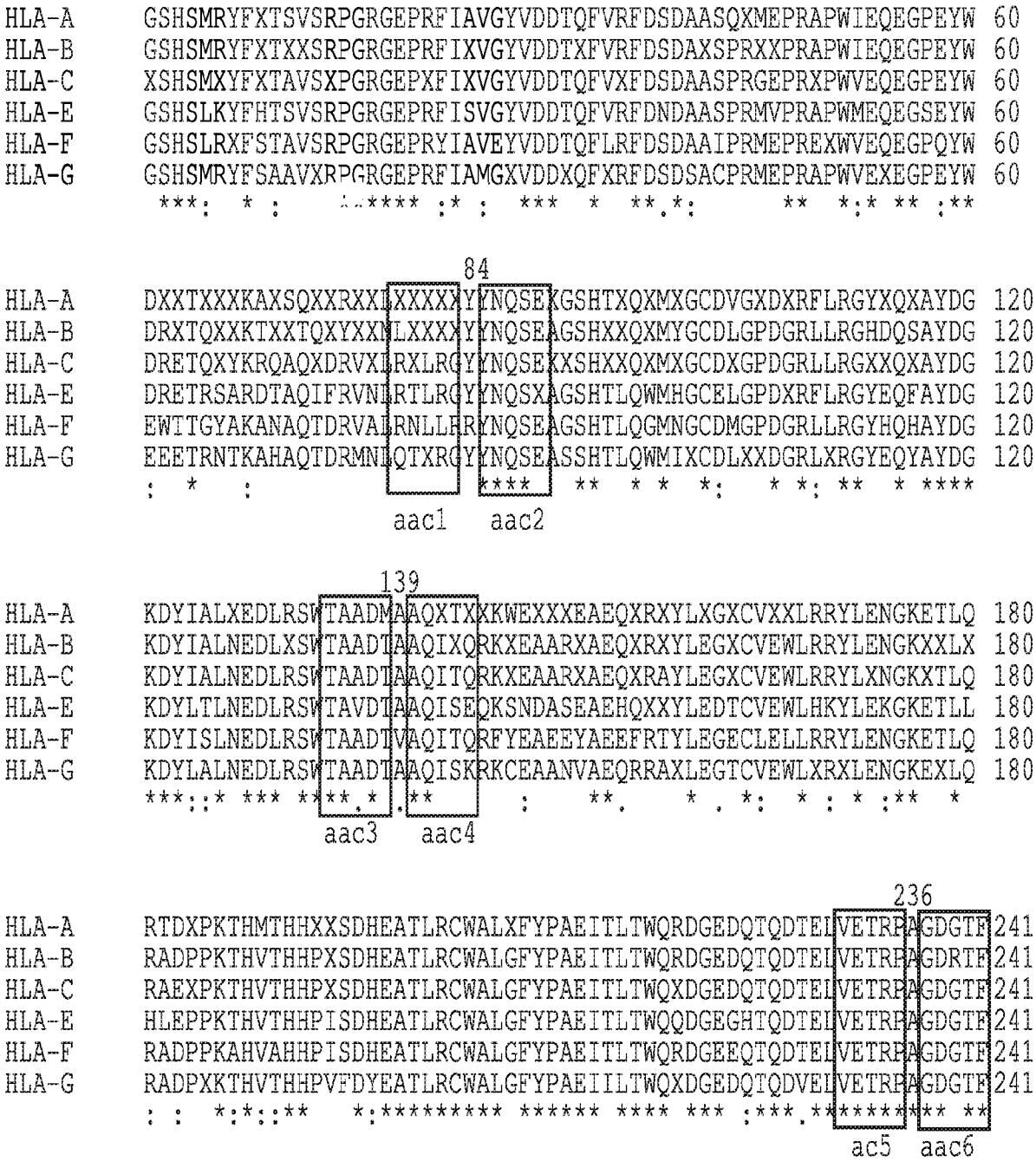

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HLA-C XSHSMXYFXTAVSXPGRGEPXFIXVGYVDDTQFVXFDSDAASPRGEPRXPWVEQEGPEYW 60
HLA-E GSHSLKYFHTSVSRPGRGEPRFISVGYVDDTQFVRFDNDAASPRMVPRAPWMEQEGSEYW 60
HLA-F GSHSLRXFSTAVSRPGRGEPRYIAVEYVDDTQFLRFDSDAAIPRMEPREXWVEQEGPQYW 60
HLA-G GSHSMRYFSAAVXRPGRGEPRFIAMGXVDDXQFXRFDSDSACPRMEPRAPWVEXEGPEYW 60
84
HLA-A DXXTXXXKAXSQXXRXXLXXXXXYYNQSEKGSHTXQXMXGCDVGXDXRFLRGYXQXAYDG 120
HLA-B DRXTQXXKTXXTQXYXXNLXXXXYYNQSEAGSHXXQXMYGCDLGPDGRLLRGHDQSAYDG 120
HLA-C DRETQXYKRQAQXDRVXLRXLRGYYNQSEKXSHXXQXMXGCDXGPDGRLLRGXXQXAYDG 120
HLA-E DRETRSARDTAQIFRVNLRTLRGYYNQSXAGSHTLQWMHGCELGPDXRFLRGYEQFAYDG 120
HLA-F EWTTGYAKANAQTDRVALRNLLRRYNQSEAGSHTLQGMNGCDMGPDGRLLRGYHQHAYDG 120
HLA-G EEETRNTKAHAQTDRMNLQTXRGYYNQSEASSHTLQWMIXCDLXXDGRLXRGYEQYAYDG 120
aac1
aac2
139
HLA-A KDYIALXEDLRSWTAADMAAQXTXKKWEXXXEAEQXRXYLXGXCVXXLRRYLENGKETLQ 180
HLA-B KDYIALNEDLXSWTAADTAAQIXQRKXEAARXAEQXRXYLEGXCVEWLRRYLENGKXXLX 180
HLA-C KDYIALNEDLRSWTAADTAAQITQRKXEAARXAEQXRAYLEGXCVEWLRRYLXNGKXTLQ 180
HLA-E KDYLTLNEDLRSWTAVDTAAQISEQKSNDASEAEHQXXYLEDTCVEWLHKYLEKGKETLL 180
HLA-F KDYISLNEDLRSWTAADTAAQITQRFYEAEEYAEEFRTYLEGECLELLRRYLENGKETLQ 180
HLA-G KDYLALNEDLRSWTAADTAAQISKRKCEAANVAEQRRAXLEGTCVEWLXRXLENGKEXLQ 180
aac3
aac4
236
HLA-A RTDXPKTHMTHHXXSDHEATLRCWALXFYPAEITLTWQRDGEDQTQDTELVETRPAGDGTF 241
HLA-B RADPPKTHVTHHPXSDHEATLRCWALGFYPAEITLTWQRDGEDQTQDTELVETRPAGDRTF 241
HLA-C RAEXPKTHVTHHPXSDHEATLRCWALGFYPAEITLTWQXDGEDQTQDTELVETRPAGDGTF 241
HLA-E HLEPPKTHVTHHPISDHEATLRCWALGFYPAEITLTWQQDGEGHTQDTELVETRPAGDGTF 241
HLA-F RADPPKAHVAHHPISDHEATLRCWALGFYPAEITLTWQRDGEEQTQDTELVETRPAGDGTF 241
HLA-G RADPXKTHVTHHPVFDYEATLRCWALGFYPAEIILTWQXDGEDQTQDVELVETRPAGDGTF 241
ac5
aac6
HLA-A QKWAXVVVPSGXEQRYTCHVQHEGLPKPLTLRWEX--------- 276
HLA-B QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWEP--------- 276
HLA-C QKWAAVXVPSGXEQRYTCHXQHEGLXEPLTLXWXP--------- 276
HLA-E QKWAAVVVPSGEEXRYTCHVQHEGLXEPVTLRWKPASQPTIPI 284
HLA-F QKWAAVVVPXGEEQRYTCHVQHEGLPQPLILRWEQSXQPTIPI 284
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FIG. 12A

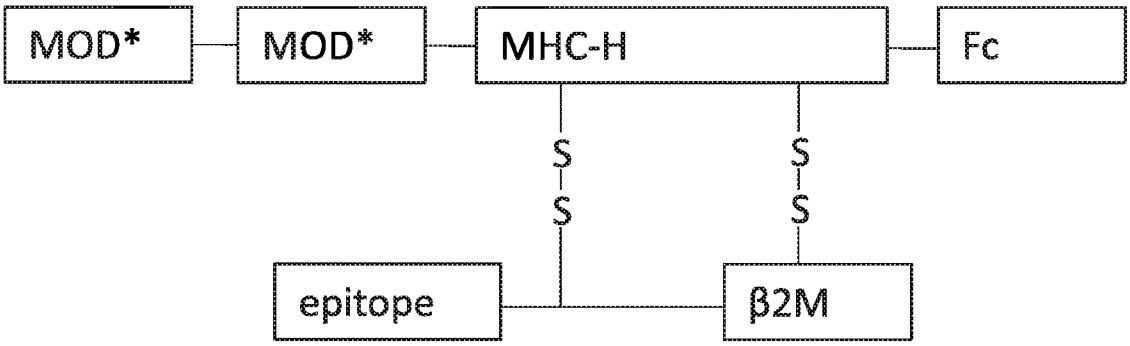


FIG. 12B

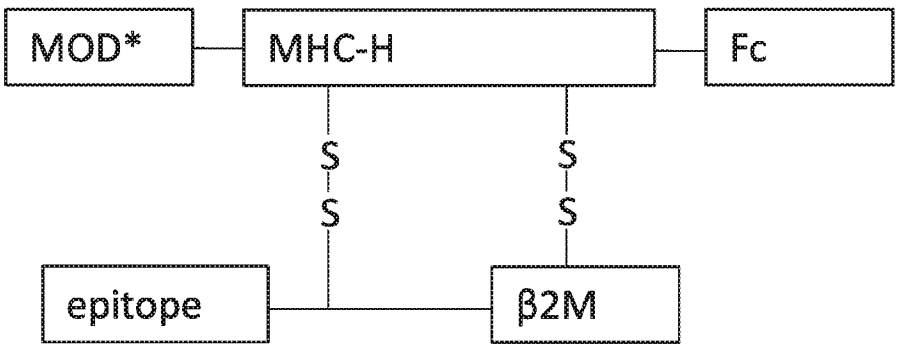


FIG. 12C

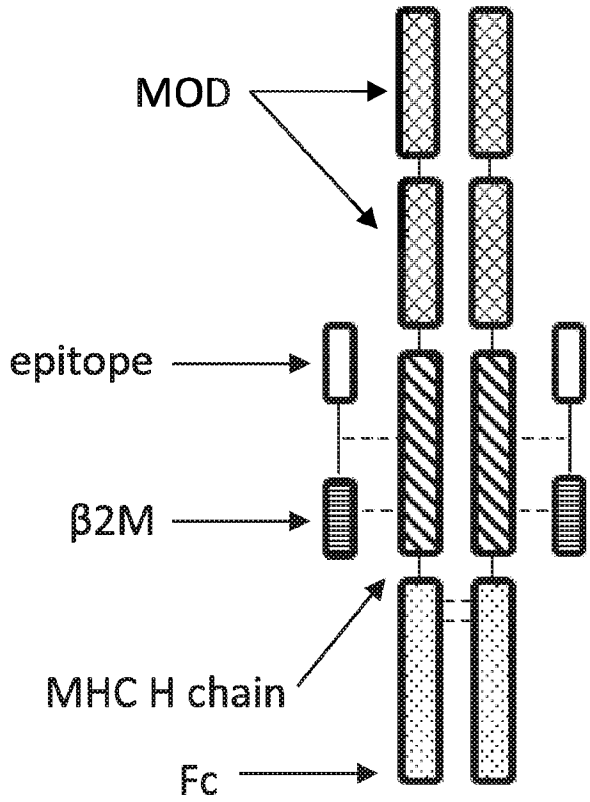


FIG. 12D

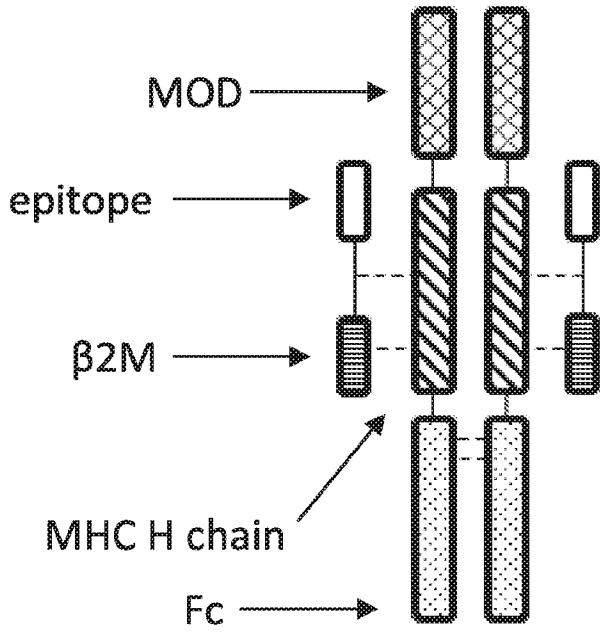


FIG. 13A

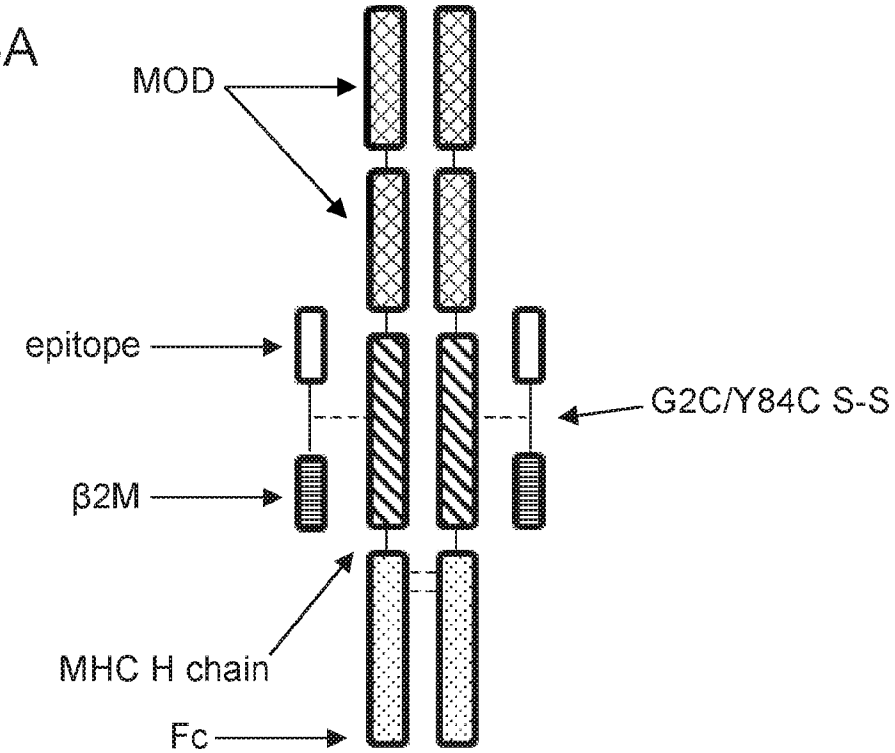


FIG. 13B

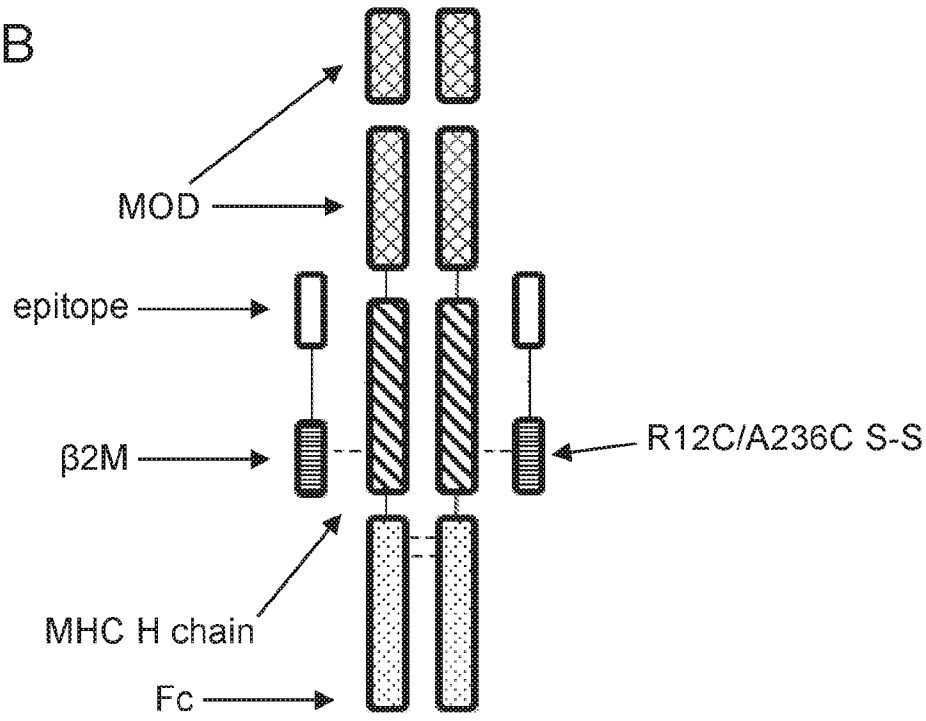


FIG. 13C

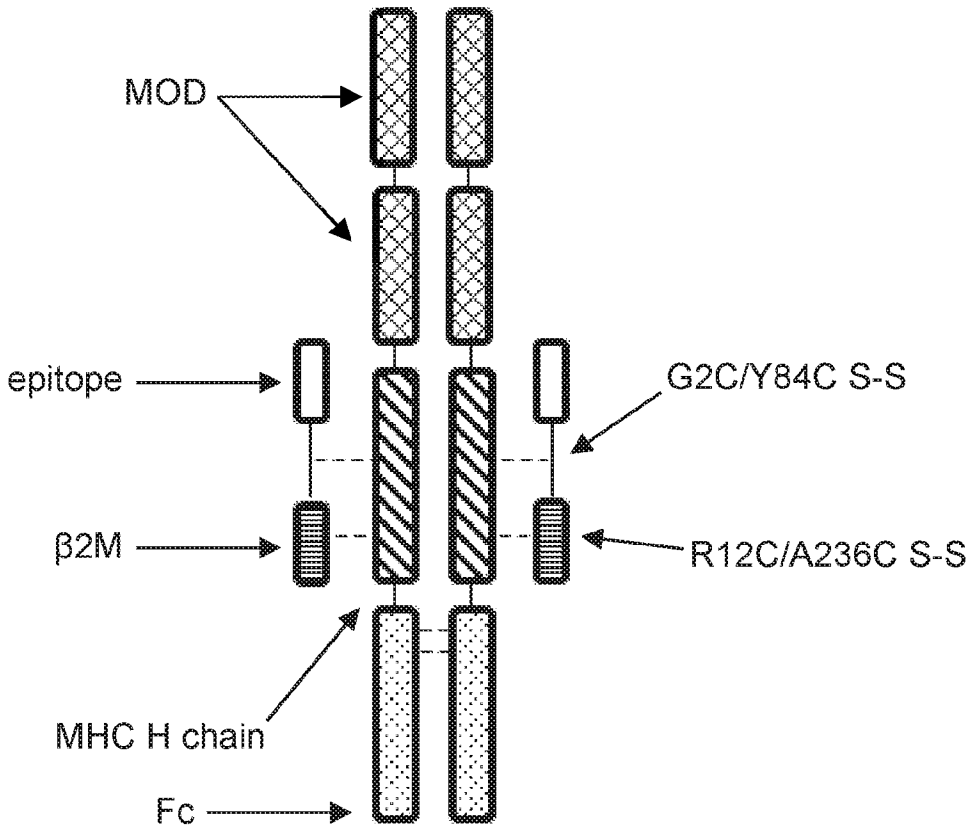
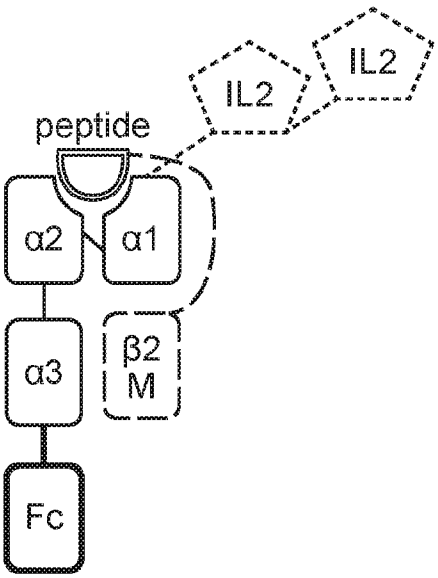
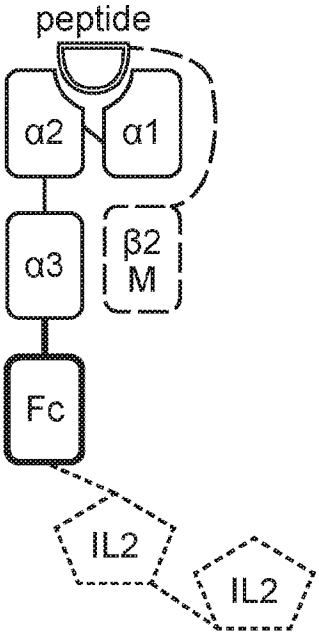


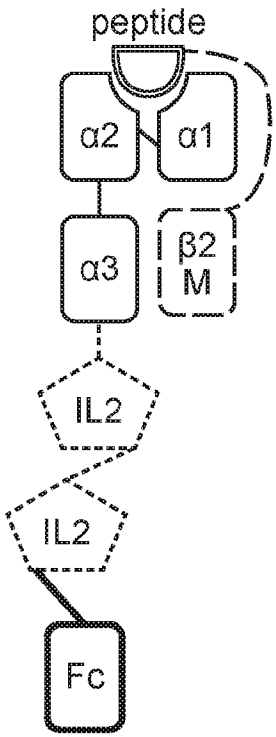
FIG. 14



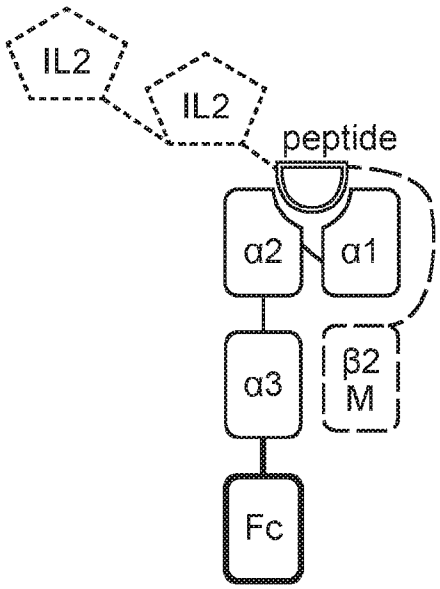
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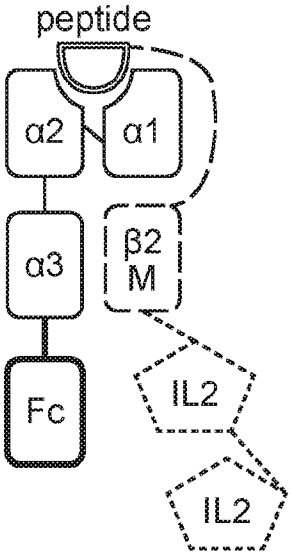
Position 3



Position 2



Position 4



Position 5

SEQUENCE LISTING

<110> Cue Biopharma, Inc.
Seidel III, Ronald D
Chaparro, Rodolfo J

<120> Multimeric T-Cell Modulatory Polypeptides and Methods of Use Thereof

<130> CUEB-117WO

<150> US 62/782,205
<151> 2018-12-19

<150> US 62/814,707
<151> 2019-03-06

<160> 462

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Asn Ala Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr
20 25 30

Gly Ser Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu
35 40 45

Asp Leu Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile
50 55 60

Ile Gln Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser
65 70 75 80

Tyr Arg Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn
85 90 95

Ala Ala Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr
100 105 110

```
Arg Cys Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val
        115                 120                 125

Lys Val Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val
    130                 135                 140

Asp Pro Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr
145                 150                 155                 160

Pro Lys Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser
                165                 170                 175

Gly Lys Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn
            180                 185                 190

Val Thr Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr
        195                 200                 205

Cys Thr Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu
    210                 215                 220

Val Ile Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile Cys Leu Thr
225                 230                 235                 240

Leu Ser Pro Ser Thr
                245
```

<210> 2
<211> 219
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<213> Homo sapiens

<400> 2

```
Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
1               5                   10                  15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
            20                  25                  30

Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
```

```
        35                  40                  45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
    50                  55                  60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65                  70                  75                  80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
                85                  90                  95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
            100                 105                 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
        115                 120                 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
    130                 135                 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145                 150                 155                 160

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
                165                 170                 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
            180                 185                 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
        195                 200                 205

Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
    210                 215
```

<210> 3
<211> 268
<212> PRT
<213> Homo sapiens

<400> 3

```
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1               5                  10                  15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
            20                  25                  30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
        35                  40                  45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
    50                  55                  60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65                  70                  75                  80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85                  90                  95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100                 105                 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115                 120                 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130                 135                 140

Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly Leu Leu Gly Ser
145                 150                 155                 160

Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys Ser Arg Ala Ala
                165                 170                 175

Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro Leu Lys Glu Asp
            180                 185                 190

Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly Glu Leu Asp Phe
        195                 200                 205

Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro Cys Val Pro Glu
    210                 215                 220
```

```
Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly Met Gly Thr Ser
225                 230                 235                 240


Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg Ser Ala Gln Pro
                245                 250                 255


Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu
            260                 265
```

<210> 4
<211> 208
<212> PRT
<213> Homo sapiens

<400> 4

```
Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15


Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30


Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45


Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60


Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80


Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95


Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110


Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125


Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
```

```
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205
```

<210> 5
<211> 220
<212> PRT
<213> Homo sapiens

<400> 5

```
Met Leu Arg Leu Leu Leu Ala Leu Asn Leu Phe Pro Ser Ile Gln Val
1               5                   10                  15

Thr Gly Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala Tyr
            20                  25                  30

Asp Asn Ala Val Asn Leu Ser Cys Lys Tyr Ser Tyr Asn Leu Phe Ser
        35                  40                  45

Arg Glu Phe Arg Ala Ser Leu His Lys Gly Leu Asp Ser Ala Val Glu
    50                  55                  60

Val Cys Val Val Tyr Gly Asn Tyr Ser Gln Gln Leu Gln Val Tyr Ser
65                  70                  75                  80

Lys Thr Gly Phe Asn Cys Asp Gly Lys Leu Gly Asn Glu Ser Val Thr
                85                  90                  95

Phe Tyr Leu Gln Asn Leu Tyr Val Asn Gln Thr Asp Ile Tyr Phe Cys
            100                 105                 110
```

```
Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser
        115                 120                 125

Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro
    130                 135                 140

Leu Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly
145                 150                 155                 160

Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile
                165                 170                 175

Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met
            180                 185                 190

Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro
        195                 200                 205

Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
    210                 215                 220
```

<210> 6
<211> 123
<212> PRT
<213> Homo sapiens

<400> 6

```
Met Leu Arg Leu Leu Leu Ala Leu Asn Leu Phe Pro Ser Ile Gln Val
1               5                   10                  15

Thr Gly Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala Tyr
            20                  25                  30

Asp Asn Ala Val Asn Leu Ser Trp Lys His Leu Cys Pro Ser Pro Leu
        35                  40                  45

Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly
    50                  55                  60

Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe
65                  70                  75                  80
```

```
Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn
                85                  90                  95

Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr
            100                 105                 110

Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
        115                 120
```

<210> 7
<211> 101
<212> PRT
<213> Homo sapiens

<400> 7

```
Met Leu Arg Leu Leu Leu Ala Leu Asn Leu Phe Pro Ser Ile Gln Val
1               5                   10                  15

Thr Gly Lys His Leu Cys Pro Ser Pro Leu Phe Pro Gly Pro Ser Lys
            20                  25                  30

Pro Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser
        35                  40                  45

Leu Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg
    50                  55                  60

Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro
65                  70                  75                  80

Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe
                85                  90                  95

Ala Ala Tyr Arg Ser
            100
```

<210> 8
<211> 224
<212> PRT
<213> Homo sapiens

<400> 8

```
Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                  10                  15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
```

210 215 220

<210> 9
<211> 110
<212> PRT
<213> Homo sapiens

<400> 9

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 10
<211> 254
<212> PRT
<213> Homo sapiens

<400> 10

Met Glu Tyr Ala Ser Asp Ala Ser Leu Asp Pro Glu Ala Pro Trp Pro
1 5 10 15

Pro Ala Pro Arg Ala Arg Ala Cys Arg Val Leu Pro Trp Ala Leu Val
20 25 30

Ala Gly Leu Leu Leu Leu Leu Leu Leu Ala Ala Ala Cys Ala Val Phe

```
        35                  40                  45

Leu Ala Cys Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser
    50                  55                  60

Ala Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp
65                  70                  75                  80

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
                85                  90                  95

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            100                 105                 110

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        115                 120                 125

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    130                 135                 140

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
145                 150                 155                 160

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                165                 170                 175

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            180                 185                 190

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        195                 200                 205

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    210                 215                 220

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
225                 230                 235                 240

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                245                 250
```

<210> 11
<211> 174
<212> PRT
<213> Homo sapiens

<400> 11

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15


Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125


Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140


Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 12
<211> 175

<212> PRT
<213> Homo sapiens

<400> 12

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1 5 10 15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
20 25 30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
50 55 60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65 70 75 80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
85 90 95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
100 105 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
115 120 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
130 135 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145 150 155 160

Val Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170 175

<210> 13
<211> 167
<212> PRT
<213> Homo sapiens

<400> 13

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1 5 10 15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
20 25 30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
50 55 60

Phe Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly
65 70 75 80

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
85 90 95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
100 105 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
115 120 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
130 135 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145 150 155 160

Val Thr Pro Glu Ile Pro Ala
165

<210> 14
<211> 255
<212> PRT
<213> Homo sapiens

<400> 14

Met Gly Asn Ser Cys Tyr Asn Ile Val Ala Thr Leu Leu Leu Val Leu

```
1               5                   10                  15

Asn Phe Glu Arg Thr Arg Ser Leu Gln Asp Pro Cys Ser Asn Cys Pro
            20                  25                  30

Ala Gly Thr Phe Cys Asp Asn Asn Arg Asn Gln Ile Cys Ser Pro Cys
        35                  40                  45

Pro Pro Asn Ser Phe Ser Ser Ala Gly Gly Gln Arg Thr Cys Asp Ile
    50                  55                  60

Cys Arg Gln Cys Lys Gly Val Phe Arg Thr Arg Lys Glu Cys Ser Ser
65                  70                  75                  80

Thr Ser Asn Ala Glu Cys Asp Cys Thr Pro Gly Phe His Cys Leu Gly
                85                  90                  95

Ala Gly Cys Ser Met Cys Glu Gln Asp Cys Lys Gln Gly Gln Glu Leu
            100                 105                 110

Thr Lys Lys Gly Cys Lys Asp Cys Cys Phe Gly Thr Phe Asn Asp Gln
        115                 120                 125

Lys Arg Gly Ile Cys Arg Pro Trp Thr Asn Cys Ser Leu Asp Gly Lys
    130                 135                 140

Ser Val Leu Val Asn Gly Thr Lys Glu Arg Asp Val Val Cys Gly Pro
145                 150                 155                 160

Ser Pro Ala Asp Leu Ser Pro Gly Ala Ser Ser Val Thr Pro Pro Ala
                165                 170                 175

Pro Ala Arg Glu Pro Gly His Ser Pro Gln Ile Ile Ser Phe Phe Leu
            180                 185                 190

Ala Leu Thr Ser Thr Ala Leu Leu Phe Leu Leu Phe Phe Leu Thr Leu
        195                 200                 205

Arg Phe Ser Val Val Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
    210                 215                 220
```

```
Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
225                 230                 235                 240


Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
                245                 250                 255


<210>  15
<211>  133
<212>  PRT
<213>  Homo sapiens

<400>  15

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1               5                   10                  15


Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
            20                  25                  30


Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
        35                  40                  45


Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50                  55                  60


Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65                  70                  75                  80


Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85                  90                  95


Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100                 105                 110


Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
        115                 120                 125


Ile Ser Thr Leu Thr
    130


<210>  16
<211>  251
```

<212> PRT
<213> Homo sapiens

<400> 16

Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile Pro His Ala Thr Phe Lys
1 5 10 15

Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn Cys Glu Cys Lys Arg
20 25 30

Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr Met Leu Cys Thr Gly
35 40 45

Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys Gln Cys Thr Ser Ser
50 55 60

Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro Gln Pro Glu Glu Gln
65 70 75 80

Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro Met Gln Pro Val Asp
85 90 95

Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro Pro Pro Trp Glu Asn
100 105 110

Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val Gly Gln Met Val Tyr
115 120 125

Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His Arg Gly Pro Ala Glu
130 135 140

Ser Val Cys Lys Met Thr His Gly Lys Thr Arg Trp Thr Gln Pro Gln
145 150 155 160

Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln Phe Pro Gly Glu Glu
165 170 175

Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu Ser Glu Thr Ser Cys
180 185 190

Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr Glu Met Ala Ala Thr

```
        195                 200                 205

Met Glu Thr Ser Ile Phe Thr Thr Glu Tyr Gln Val Ala Val Ala Gly
    210                 215                 220

Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu Ser Gly Leu Thr Trp
225                 230                 235                 240

Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
                245                 250
```

<210> 17
<211> 524
<212> PRT
<213> Homo sapiens

<400> 17

```
Val Asn Gly Thr Ser Gln Phe Thr Cys Phe Tyr Asn Ser Arg Ala Asn
1               5                   10                  15

Ile Ser Cys Val Trp Ser Gln Asp Gly Ala Leu Gln Asp Thr Ser Cys
            20                  25                  30

Gln Val His Ala Trp Pro Asp Arg Arg Arg Trp Asn Gln Thr Cys Glu
        35                  40                  45

Leu Leu Pro Val Ser Gln Ala Ser Trp Ala Cys Asn Leu Ile Leu Gly
    50                  55                  60

Ala Pro Asp Ser Gln Lys Leu Thr Thr Val Asp Ile Val Thr Leu Arg
65                  70                  75                  80

Val Leu Cys Arg Glu Gly Val Arg Trp Arg Val Met Ala Ile Gln Asp
                85                  90                  95

Phe Lys Pro Phe Glu Asn Leu Arg Leu Met Ala Pro Ile Ser Leu Gln
            100                 105                 110

Val Val His Val Glu Thr His Arg Cys Asn Ile Ser Trp Glu Ile Ser
        115                 120                 125
```

```
Gln Ala Ser His Tyr Phe Glu Arg His Leu Glu Phe Glu Ala Arg Thr
    130                 135                 140

Leu Ser Pro Gly His Thr Trp Glu Glu Ala Pro Leu Leu Thr Leu Lys
145                 150                 155                 160

Gln Lys Gln Glu Trp Ile Cys Leu Glu Thr Leu Thr Pro Asp Thr Gln
                165                 170                 175

Tyr Glu Phe Gln Val Arg Val Lys Pro Leu Gln Gly Glu Phe Thr Thr
            180                 185                 190

Trp Ser Pro Trp Ser Gln Pro Leu Ala Phe Arg Thr Lys Pro Ala Ala
        195                 200                 205

Leu Gly Lys Asp Thr Ile Pro Trp Leu Gly His Leu Leu Val Gly Leu
    210                 215                 220

Ser Gly Ala Phe Gly Phe Ile Ile Leu Val Tyr Leu Leu Ile Asn Cys
225                 230                 235                 240

Arg Asn Thr Gly Pro Trp Leu Lys Lys Val Leu Lys Cys Asn Thr Pro
                245                 250                 255

Asp Pro Ser Lys Phe Phe Ser Gln Leu Ser Ser Glu His Gly Gly Asp
            260                 265                 270

Val Gln Lys Trp Leu Ser Ser Pro Phe Pro Ser Ser Ser Phe Ser Pro
        275                 280                 285

Gly Gly Leu Ala Pro Glu Ile Ser Pro Leu Glu Val Leu Glu Arg Asp
    290                 295                 300

Lys Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala
305                 310                 315                 320

Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly
                325                 330                 335

Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln
            340                 345                 350
```

```
Val Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly
        355                 360                 365

Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu
    370                 375                 380

Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu
385                 390                 395                 400

Leu Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr
                405                 410                 415

Ala Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu
            420                 425                 430

Gln Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro
        435                 440                 445

Thr Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu
    450                 455                 460

Val Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu
465                 470                 475                 480

Gly Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg
                485                 490                 495

Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
            500                 505                 510

Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        515                 520
```

<210> 18
<211> 347
<212> PRT
<213> Homo sapiens

<400> 18

```
Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly Asn Glu Asp Thr Thr Ala
```

```
1               5                   10                  15

Asp Phe Phe Leu Thr Thr Met Pro Thr Asp Ser Leu Ser Val Ser Thr
            20                  25                  30

Leu Pro Leu Pro Glu Val Gln Cys Phe Val Phe Asn Val Glu Tyr Met
        35                  40                  45

Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro Gln Pro Thr Asn Leu Thr
    50                  55                  60

Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn Asp Lys Val Gln Lys Cys
65                  70                  75                  80

Ser His Tyr Leu Phe Ser Glu Glu Ile Thr Ser Gly Cys Gln Leu Gln
                85                  90                  95

Lys Lys Glu Ile His Leu Tyr Gln Thr Phe Val Val Gln Leu Gln Asp
            100                 105                 110

Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln Met Leu Lys Leu Gln Asn
        115                 120                 125

Leu Val Ile Pro Trp Ala Pro Glu Asn Leu Thr Leu His Lys Leu Ser
    130                 135                 140

Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn Arg Phe Leu Asn His Cys
145                 150                 155                 160

Leu Glu His Leu Val Gln Tyr Arg Thr Asp Trp Asp His Ser Trp Thr
                165                 170                 175

Glu Gln Ser Val Asp Tyr Arg His Lys Phe Ser Leu Pro Ser Val Asp
            180                 185                 190

Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg Ser Arg Phe Asn Pro Leu
        195                 200                 205

Cys Gly Ser Ala Gln His Trp Ser Glu Trp Ser His Pro Ile His Trp
    210                 215                 220
```

```
Gly Ser Asn Thr Ser Lys Glu Asn Pro Phe Leu Phe Ala Leu Glu Ala
225                 230                 235                 240


Val Val Ile Ser Val Gly Ser Met Gly Leu Ile Ile Ser Leu Leu Cys
                245                 250                 255


Val Tyr Phe Trp Leu Glu Arg Thr Met Pro Arg Ile Pro Thr Leu Lys
            260                 265                 270


Asn Leu Glu Asp Leu Val Thr Glu Tyr His Gly Asn Phe Ser Ala Trp
        275                 280                 285


Ser Gly Val Ser Lys Gly Leu Ala Glu Ser Leu Gln Pro Asp Tyr Ser
    290                 295                 300


Glu Arg Leu Cys Leu Val Ser Glu Ile Pro Pro Lys Gly Gly Ala Leu
305                 310                 315                 320


Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn Gln His Ser Pro Tyr Trp
                325                 330                 335


Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu Thr
            340                 345


<210>  19
<211>  119
<212>  PRT
<213>  Homo sapiens

<400>  19

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1               5                   10                  15


Gly Leu Glu Ala Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg
            20                  25                  30


His Pro Ala Glu Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser
        35                  40                  45


Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu
    50                  55                  60
```

```
Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp
65                  70                  75                  80


Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp
                85                  90                  95


Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile
            100                 105                 110


Val Lys Trp Asp Arg Asp Met
        115


<210>  20
<211>  119
<212>  PRT
<213>  Macaca mulatta

<400>  20

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1               5                   10                  15


Gly Leu Glu Ala Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg
            20                  25                  30


His Pro Pro Glu Asn Gly Lys Pro Asn Phe Leu Asn Cys Tyr Val Ser
        35                  40                  45


Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu
    50                  55                  60


Lys Met Gly Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp
65                  70                  75                  80


Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Asn Glu Lys Asp
                85                  90                  95


Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gly Pro Arg Thr
            100                 105                 110


Val Lys Trp Asp Arg Asp Met
```

115

<210> 21
<211> 118
<212> PRT
<213> Bos Taurus

<400> 21

Met Ala Arg Phe Val Ala Leu Val Leu Leu Gly Leu Leu Ser Leu Ser
1 5 10 15

Gly Leu Asp Ala Ile Gln Arg Pro Pro Lys Ile Gln Val Tyr Ser Arg
20 25 30

His Pro Pro Glu Asp Gly Lys Pro Asn Tyr Leu Asn Cys Tyr Val Tyr
35 40 45

Gly Phe His Pro Pro Gln Ile Glu Ile Asp Leu Leu Lys Asn Gly Glu
50 55 60

Lys Ile Lys Ser Glu Gln Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser
65 70 75 80

Phe Tyr Leu Leu Ser His Ala Glu Phe Thr Pro Asn Ser Lys Asp Gln
85 90 95

Tyr Ser Cys Arg Val Lys His Val Thr Leu Glu Gln Pro Arg Ile Val
100 105 110

Lys Trp Asp Arg Asp Leu
115

<210> 22
<211> 119
<212> PRT
<213> Mus musculus

<400> 22

Met Ala Arg Ser Val Thr Leu Val Phe Leu Val Leu Val Ser Leu Thr
1 5 10 15

Gly Leu Tyr Ala Ile Gln Lys Thr Pro Gln Ile Gln Val Tyr Ser Arg

```
            20                  25                  30

His Pro Pro Glu Asn Gly Lys Pro Asn Ile Leu Asn Cys Tyr Val Thr
        35                  40                  45

Gln Phe His Pro Pro His Ile Glu Ile Gln Met Leu Lys Asn Gly Lys
    50                  55                  60

Lys Ile Pro Lys Val Glu Met Ser Asp Met Ser Phe Ser Lys Asp Trp
65                  70                  75                  80

Ser Phe Tyr Ile Leu Ala His Thr Glu Phe Thr Pro Thr Glu Thr Asp
                85                  90                  95

Thr Tyr Ala Cys Arg Val Lys His Ala Ser Met Ala Glu Pro Lys Thr
            100                 105                 110

Val Tyr Trp Asp Arg Asp Met
        115
```

<210> 23
<211> 365
<212> PRT
<213> Homo sapiens

<400> 23

```
Met Ala Val Met Ala Pro Arg Thr Leu Leu Leu Leu Leu Ser Gly Ala
1               5                   10                  15

Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
            20                  25                  30

Phe Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
        35                  40                  45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50                  55                  60

Ala Ser Gln Lys Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65                  70                  75                  80
```

```
Pro Glu Tyr Trp Asp Gln Glu Thr Arg Asn Met Lys Ala His Ser Gln
                85                  90                  95

Thr Asp Arg Ala Asn Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
            100                 105                 110

Glu Asp Gly Ser His Thr Ile Gln Ile Met Tyr Gly Cys Asp Val Gly
        115                 120                 125

Pro Asp Gly Arg Phe Leu Arg Gly Tyr Arg Gln Asp Ala Tyr Asp Gly
    130                 135                 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145                 150                 155                 160

Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Val His Ala
                165                 170                 175

Ala Glu Gln Arg Arg Val Tyr Leu Glu Gly Arg Cys Val Asp Gly Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
        195                 200                 205

Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
            260                 265                 270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Leu Ser Ser Gln Pro
    290                 295                 300
```

```
Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala
305                 310                 315                 320


Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser
                325                 330                 335


Ser Asp Arg Lys Gly Gly Ser Tyr Thr Gln Ala Ala Ser Ser Asp Ser
            340                 345                 350


Ala Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
        355                 360                 365
```

<210> 24
<211> 365
<212> PRT
<213> Homo sapiens

<400> 24

```
Met Ala Val Met Ala Pro Arg Thr Leu Leu Leu Leu Leu Ser Gly Ala
1               5                   10                  15


Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
            20                  25                  30


Tyr Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
        35                  40                  45


Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50                  55                  60


Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65                  70                  75                  80


Pro Glu Tyr Trp Asp Gln Glu Thr Arg Asn Val Lys Ala Gln Ser Gln
                85                  90                  95


Thr Asp Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
            100                 105                 110


Glu Asp Gly Ser His Thr Ile Gln Ile Met Tyr Gly Cys Asp Val Gly
```

```
        115                 120                 125

Pro Asp Gly Arg Phe Leu Arg Gly Tyr Arg Gln Asp Ala Tyr Asp Gly
    130                 135                 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145                 150                 155                 160

Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Ala His Ala
                165                 170                 175

Ala Glu Gln Gln Arg Ala Tyr Leu Glu Gly Arg Cys Val Glu Trp Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
        195                 200                 205

Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
            260                 265                 270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Leu Ser Ser Gln Pro
    290                 295                 300

Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala
305                 310                 315                 320

Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser
                325                 330                 335
```

Ser Asp Arg Lys Gly Gly Ser Tyr Thr Gln Ala Ala Ser Ser Asp Ser
340 345 350

Ala Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
355 360 365

<210> 25
<211> 365
<212> PRT
<213> Homo sapiens

<400> 25

Met Ala Val Met Ala Pro Arg Thr Leu Val Leu Leu Leu Ser Gly Ala
1 5 10 15

Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
20 25 30

Ser Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
35 40 45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
50 55 60

Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65 70 75 80

Pro Glu Tyr Trp Asp Glu Glu Thr Gly Lys Val Lys Ala His Ser Gln
85 90 95

Thr Asp Arg Glu Asn Leu Arg Ile Ala Leu Arg Tyr Tyr Asn Gln Ser
100 105 110

Glu Ala Gly Ser His Thr Leu Gln Met Met Phe Gly Cys Asp Val Gly
115 120 125

Ser Asp Gly Arg Phe Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly
130 135 140

Lys Asp Tyr Ile Ala Leu Lys Glu Asp Leu Arg Ser Trp Thr Ala Ala
145 150 155 160

```
Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Ala His Val
                165                 170                 175

Ala Glu Gln Gln Arg Ala Tyr Leu Glu Gly Thr Cys Val Asp Gly Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
        195                 200                 205

Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
            260                 265                 270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro
    290                 295                 300

Thr Val Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala
305                 310                 315                 320

Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Asn Ser
                325                 330                 335

Ser Asp Arg Lys Gly Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser
            340                 345                 350

Ala Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
        355                 360                 365
```

<210> 26
<211> 365
<212> PRT
<213> Homo sapiens

<400> 26

```
Met Ala Val Met Ala Pro Arg Thr Leu Leu Leu Leu Leu Leu Gly Ala
1               5                   10                  15


Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
            20                  25                  30


Thr Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
        35                  40                  45


Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50                  55                  60


Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65                  70                  75                  80


Pro Glu Tyr Trp Asp Arg Asn Thr Arg Asn Val Lys Ala His Ser Gln
                85                  90                  95


Ile Asp Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
            100                 105                 110


Glu Ala Gly Ser His Thr Ile Gln Met Met Tyr Gly Cys Asp Val Gly
        115                 120                 125


Ser Asp Gly Arg Phe Leu Arg Gly Tyr Gln Gln Asp Ala Tyr Asp Gly
    130                 135                 140


Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145                 150                 155                 160


Asp Met Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Val
                165                 170                 175


Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu
            180                 185                 190
```

```
Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
        195                 200                 205

Pro Lys Thr His Met Thr His His Ala Val Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Ser Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ser Val Val
            260                 265                 270

Val Pro Ser Gly Gln Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro
    290                 295                 300

Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Phe Gly Ala
305                 310                 315                 320

Val Phe Ala Gly Ala Val Val Ala Ala Val Arg Trp Arg Arg Lys Ser
                325                 330                 335

Ser Asp Arg Lys Gly Gly Ser Tyr Ser Gln Ala Ala Ser Ser Asp Ser
            340                 345                 350

Ala Gln Gly Ser Asp Met Ser Leu Thr Ala Cys Lys Val
        355                 360                 365
```

<210> 27
<211> 362
<212> PRT
<213> Homo sapiens

<400> 27

```
Met Leu Val Met Ala Pro Arg Thr Val Leu Leu Leu Leu Ser Ala Ala
1               5                   10                  15
```

```
Leu Ala Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
            20                  25                  30

Tyr Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser
        35                  40                  45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50                  55                  60

Ala Ser Pro Arg Glu Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65                  70                  75                  80

Pro Glu Tyr Trp Asp Arg Asn Thr Gln Ile Tyr Lys Ala Gln Ala Gln
                85                  90                  95

Thr Asp Arg Glu Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
            100                 105                 110

Glu Ala Gly Ser His Thr Leu Gln Ser Met Tyr Gly Cys Asp Val Gly
        115                 120                 125

Pro Asp Gly Arg Leu Leu Arg Gly His Asp Gln Tyr Ala Tyr Asp Gly
    130                 135                 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145                 150                 155                 160

Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu
                165                 170                 175

Ala Glu Gln Arg Arg Ala Tyr Leu Glu Gly Glu Cys Val Glu Trp Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Asp Lys Leu Glu Arg Ala Asp Pro
        195                 200                 205

Pro Lys Thr His Val Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210                 215                 220
```

```
Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240


Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255


Thr Arg Pro Ala Gly Asp Arg Thr Phe Gln Lys Trp Ala Ala Val Val
            260                 265                 270


Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275                 280                 285


Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Ser
    290                 295                 300


Thr Val Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val
305                 310                 315                 320


Val Val Ile Gly Ala Val Val Ala Ala Val Met Cys Arg Arg Lys Ser
                325                 330                 335


Ser Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys Ser Asp Ser
            340                 345                 350


Ala Gln Gly Ser Asp Val Ser Leu Thr Ala
        355                 360


<210>  28
<211>  366
<212>  PRT
<213>  Homo sapiens

<400>  28

Met Arg Val Met Ala Pro Arg Ala Leu Leu Leu Leu Leu Ser Gly Gly
1               5                   10                  15


Leu Ala Leu Thr Glu Thr Trp Ala Cys Ser His Ser Met Arg Tyr Phe
            20                  25                  30


Asp Thr Ala Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser
        35                  40                  45
```

```
Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50                  55                  60

Ala Ser Pro Arg Gly Glu Pro Arg Ala Pro Trp Val Glu Gln Glu Gly
65                  70                  75                  80

Pro Glu Tyr Trp Asp Arg Glu Thr Gln Asn Tyr Lys Arg Gln Ala Gln
                85                  90                  95

Ala Asp Arg Val Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
            100                 105                 110

Glu Asp Gly Ser His Thr Leu Gln Arg Met Tyr Gly Cys Asp Leu Gly
        115                 120                 125

Pro Asp Gly Arg Leu Leu Arg Gly Tyr Asp Gln Ser Ala Tyr Asp Gly
    130                 135                 140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145                 150                 155                 160

Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Leu Glu Ala Ala Arg Ala
                165                 170                 175

Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu
            180                 185                 190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Glu Pro
        195                 200                 205

Pro Lys Thr His Val Thr His His Pro Leu Ser Asp His Glu Ala Thr
    210                 215                 220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225                 230                 235                 240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245                 250                 255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
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            260                 265                 270

Val Pro Ser Gly Gln Glu Gln Arg Tyr Thr Cys His Met Gln His Glu
        275                 280                 285

Gly Leu Gln Glu Pro Leu Thr Leu Ser Trp Glu Pro Ser Ser Gln Pro
    290                 295                 300

Thr Ile Pro Ile Met Gly Ile Val Ala Gly Leu Ala Val Leu Val Val
305                 310                 315                 320

Leu Ala Val Leu Gly Ala Val Val Thr Ala Met Met Cys Arg Arg Lys
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Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Thr Cys Lys Ala
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Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
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Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Xaa Xaa Thr
    50                  55                  60

Xaa Xaa Xaa Lys Ala Xaa Ser Gln Xaa Xaa Arg Xaa Xaa Leu Xaa Xaa
65                  70                  75                  80

Xaa Xaa Xaa Tyr Tyr Asn Gln Ser Glu Xaa Gly Ser His Thr Xaa Gln
                85                  90                  95

Xaa Met Xaa Gly Cys Asp Val Gly Xaa Asp Xaa Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Xaa Gln Xaa Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Xaa Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Xaa Thr Xaa
    130                 135                 140

Xaa Lys Trp Glu Xaa Xaa Xaa Glu Ala Glu Gln Xaa Arg Xaa Tyr Leu
145                 150                 155                 160

Xaa Gly Xaa Cys Val Xaa Xaa Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Xaa Pro Lys Thr His Met Thr His His
            180                 185                 190

Xaa Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Xaa Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Xaa Val Val Val Pro Ser Gly Xaa Glu Gln Arg
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245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Xaa
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Arg Gly Glu Pro Arg Phe Ile Xaa Val Gly Tyr Val Asp Asp Thr Xaa
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Phe Val Arg Phe Asp Ser Asp Ala Xaa Ser Pro Arg Xaa Xaa Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Xaa Thr
    50                  55                  60


Gln Xaa Xaa Lys Thr Xaa Xaa Thr Gln Xaa Tyr Xaa Xaa Asn Leu Xaa
65                  70                  75                  80


Xaa Xaa Xaa Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Xaa Xaa Gln
                85                  90                  95
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Xaa Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Xaa Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Xaa Gln
    130                 135                 140

Arg Lys Xaa Glu Ala Ala Arg Xaa Ala Glu Gln Xaa Arg Xaa Tyr Leu
145                 150                 155                 160

Glu Gly Xaa Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Xaa Xaa Leu Xaa Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
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Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
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Arg Trp Glu Pro
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20 25 30

Phe Val Xaa Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Xaa Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Xaa Tyr Lys Arg Gln Ala Gln Xaa Asp Arg Val Xaa Leu Arg Xaa
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Xaa Xaa Ser His Xaa Xaa Gln
85 90 95

Xaa Met Xaa Gly Cys Asp Xaa Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

Xaa Xaa Gln Xaa Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115   120   125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130   135   140

Arg Lys Xaa Glu Ala Ala Arg Xaa Ala Glu Gln Xaa Arg Ala Tyr Leu
145   150   155   160

Glu Gly Xaa Cys Val Glu Trp Leu Arg Arg Tyr Leu Xaa Asn Gly Lys
                165   170   175

Xaa Thr Leu Gln Arg Ala Glu Xaa Pro Lys Thr His Val Thr His His
            180   185   190

Pro Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195   200   205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Xaa Asp Gly Glu Asp Gln
    210   215   220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225   230   235   240

Phe Gln Lys Trp Ala Ala Val Xaa Val Pro Ser Gly Xaa Glu Gln Arg
                245   250   255

Tyr Thr Cys His Xaa Gln His Glu Gly Leu Xaa Glu Pro Leu Thr Leu
            260   265   270

Xaa Trp Xaa Pro
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Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Asn Asp Ala Ala Ser Pro Arg Met Val Pro Arg
35 40 45

Ala Pro Trp Met Glu Gln Glu Gly Ser Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Arg Ser Ala Arg Asp Thr Ala Gln Ile Phe Arg Val Asn Leu Arg Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Xaa Ala Gly Ser His Thr Leu Gln

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                85                  90                  95

Trp Met His Gly Cys Glu Leu Gly Pro Asp Xaa Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Glu Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Leu Thr Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Val Asp Thr Ala Ala Gln Ile Ser Glu
    130                 135                 140

Gln Lys Ser Asn Asp Ala Ser Glu Ala Glu His Gln Xaa Xaa Tyr Leu
145                 150                 155                 160

Glu Asp Thr Cys Val Glu Trp Leu His Lys Tyr Leu Glu Lys Gly Lys
                165                 170                 175

Glu Thr Leu Leu His Leu Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Gln Asp Gly Glu Gly His
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Xaa Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Xaa Glu Pro Val Thr Leu
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Arg Trp Lys Pro Ala Ser Gln Pro Thr Ile Pro Ile
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Phe Leu Arg Phe Asp Ser Asp Ala Ala Ile Pro Arg Met Glu Pro Arg
35 40 45

Glu Xaa Trp Val Glu Gln Glu Gly Pro Gln Tyr Trp Glu Trp Thr Thr
50 55 60

Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp Arg Val Ala Leu Arg Asn
65 70 75 80

Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Gly Met Asn Gly Cys Asp Met Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

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Tyr His Gln His Ala Tyr Asp Gly Lys Asp Tyr Ile Ser Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Val Ala Gln Ile Thr Gln
    130                 135                 140

Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu Glu Phe Arg Thr Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Ala His Val Ala His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Glu Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Xaa Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Gln Pro Leu Ile Leu
            260                 265                 270

Arg Trp Glu Gln Ser Xaa Gln Pro Thr Ile Pro Ile
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Arg Gly Glu Pro Arg Phe Ile Ala Met Gly Xaa Val Asp Asp Xaa Gln
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Phe Xaa Arg Phe Asp Ser Asp Ser Ala Cys Pro Arg Met Glu Pro Arg
        35   40   45

Ala Pro Trp Val Glu Xaa Glu Gly Pro Glu Tyr Trp Glu Glu Glu Thr
    50   55   60

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Arg Asn Thr Lys Ala His Ala Gln Thr Asp Arg Met Asn Leu Gln Thr
65                  70                  75                  80

Xaa Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Ser Ser His Thr Leu Gln
                85                  90                  95

Trp Met Ile Xaa Cys Asp Leu Xaa Xaa Asp Gly Arg Leu Xaa Arg Gly
            100                 105                 110

Tyr Glu Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Leu Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Ser Lys
    130                 135                 140

Arg Lys Cys Glu Ala Ala Asn Val Ala Glu Gln Arg Arg Ala Xaa Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Xaa Arg Xaa Leu Glu Asn Gly Lys
                165                 170                 175

Glu Xaa Leu Gln Arg Ala Asp Pro Xaa Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Phe Asp Tyr Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Ile Leu Thr Trp Gln Xaa Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Val Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Xaa Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Met Leu
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Arg Trp Xaa Gln Ser Ser Leu Pro Thr Ile Pro Ile
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35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Xaa Xaa Thr
50 55 60

Xaa Xaa Xaa Lys Ala Xaa Ser Gln Xaa Xaa Arg Xaa Xaa Leu Xaa Xaa
65 70 75 80

Xaa Xaa Xaa Tyr Tyr Asn Gln Ser Glu Xaa Gly Ser His Thr Xaa Gln
85 90 95

Xaa Met Xaa Gly Cys Asp Val Gly Xaa Asp Xaa Arg Phe Leu Arg Gly
100 105 110

Tyr Xaa Gln Xaa Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Xaa Glu
115 120 125

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Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Xaa Thr Xaa
    130                 135                 140

Xaa Lys Trp Glu Xaa Xaa Xaa Glu Ala Glu Gln Xaa Arg Xaa Tyr Leu
145                 150                 155                 160

Xaa Gly Xaa Cys Val Xaa Xaa Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Xaa Pro Lys Thr His Met Thr His His
            180                 185                 190

Xaa Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Xaa Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Xaa Val Val Val Pro Ser Gly Xaa Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Xaa
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Phe Val Arg Phe Asp Ser Asp Ala Xaa Ser Pro Arg Xaa Xaa Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Xaa Thr
    50                  55                  60


Gln Xaa Xaa Lys Thr Xaa Xaa Thr Gln Xaa Tyr Xaa Xaa Asn Leu Xaa
65                  70                  75                  80


Xaa Xaa Xaa Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Xaa Xaa Gln
                85                  90                  95


Xaa Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Xaa Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Xaa Gln
    130                 135                 140


Arg Lys Xaa Glu Ala Ala Arg Xaa Ala Glu Gln Xaa Arg Xaa Tyr Leu
145                 150                 155                 160


Glu Gly Xaa Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Xaa Xaa Leu Xaa Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190
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Pro Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205


Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220


Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
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Arg Trp Glu Pro
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Phe Val Xaa Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45


Xaa Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Gln Xaa Tyr Lys Arg Gln Ala Gln Xaa Asp Arg Val Xaa Leu Arg Xaa
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Xaa Xaa Ser His Xaa Xaa Gln
                85                  90                  95


Xaa Met Xaa Gly Cys Asp Xaa Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


Xaa Xaa Gln Xaa Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Xaa Glu Ala Ala Arg Xaa Ala Glu Gln Xaa Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Xaa Cys Val Glu Trp Leu Arg Arg Tyr Leu Xaa Asn Gly Lys
                165                 170                 175


Xaa Thr Leu Gln Arg Ala Glu Xaa Pro Lys Thr His Val Thr His His
            180                 185                 190


Pro Xaa Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205
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Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Xaa Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Xaa Val Pro Ser Gly Xaa Glu Gln Arg
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Tyr Thr Cys His Xaa Gln His Glu Gly Leu Xaa Glu Pro Leu Thr Leu
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Xaa Trp Xaa Pro
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Phe Val Arg Phe Asp Asn Asp Ala Ala Ser Pro Arg Met Val Pro Arg
        35                  40                  45


Ala Pro Trp Met Glu Gln Glu Gly Ser Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Arg Ser Ala Arg Asp Thr Ala Gln Ile Phe Arg Val Asn Leu Arg Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Xaa Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Trp Met His Gly Cys Glu Leu Gly Pro Asp Xaa Arg Phe Leu Arg Gly
            100                 105                 110


Tyr Glu Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Leu Thr Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Val Asp Thr Ala Ala Gln Ile Ser Glu
    130                 135                 140


Gln Lys Ser Asn Asp Ala Ser Glu Ala Glu His Gln Xaa Xaa Tyr Leu
145                 150                 155                 160


Glu Asp Thr Cys Val Glu Trp Leu His Lys Tyr Leu Glu Lys Gly Lys
                165                 170                 175


Glu Thr Leu Leu His Leu Glu Pro Pro Lys Thr His Val Thr His His
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            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Gln Asp Gly Glu Gly His
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Xaa Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Xaa Glu Pro Val Thr Leu
            260                 265                 270

Arg Trp Lys Pro Ala Ser Gln Pro Thr Ile Pro Ile
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<400> 39

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Gly Ser His Ser Leu Arg Xaa Phe Ser Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Tyr Ile Ala Val Glu Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Leu Arg Phe Asp Ser Asp Ala Ala Ile Pro Arg Met Glu Pro Arg
        35                  40                  45


Glu Xaa Trp Val Glu Gln Glu Gly Pro Gln Tyr Trp Glu Trp Thr Thr
    50                  55                  60


Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp Arg Val Ala Leu Arg Asn
65                  70                  75                  80


Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Gly Met Asn Gly Cys Asp Met Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


Tyr His Gln His Ala Tyr Asp Gly Lys Asp Tyr Ile Ser Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Val Ala Gln Ile Thr Gln
    130                 135                 140


Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu Glu Phe Arg Thr Tyr Leu
145                 150                 155                 160


Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Ala His Val Ala His His
            180                 185                 190


Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205
```

```
Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Glu Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Xaa Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Gln Pro Leu Ile Leu
            260                 265                 270

Arg Trp Glu Gln Ser Xaa Gln Pro Thr Ile Pro Ile
        275                 280
```

<210> 40
<211> 284
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (13)..(13)
<223> Xaa is S or F

<220>
<221> misc_feature
<222> (27)..(27)
<223> Xaa is Y or H

<220>
<221> misc_feature
<222> (31)..(31)
<223> Xaa is T, S, or M

<220>
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<222> (34)..(34)
<223> Xaa is L or V

<220>
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<222> (54)..(54)

<223> Xaa is Q or R

<220>
<221> misc_feature
<222> (81)..(81)
<223> Xaa is P or L

<220>
<221> misc_feature
<222> (100)..(100)
<223> Xaa is G or D

<220>
<221> misc_feature
<222> (104)..(104)
<223> Xaa is G or V

<220>
<221> misc_feature
<222> (105)..(105)
<223> Xaa is S or C

<220>
<221> misc_feature
<222> (110)..(110)
<223> Xaa is L or I

<220>
<221> misc_feature
<222> (159)..(159)
<223> Xaa is Y or H

<220>
<221> misc_feature
<222> (169)..(169)
<223> Xaa is H or R

<220>
<221> misc_feature
<222> (171)..(171)
<223> Xaa is Y or H

<220>
<221> misc_feature
<222> (178)..(178)
<223> Xaa is M or T

<220>
<221> misc_feature
<222> (185)..(185)
<223> Xaa is P or A

<220>
<221> misc_feature

<222> (219)..(219)
<223> Xaa is R, W, or Q

<220>
<221> misc_feature
<222> (258)..(258)
<223> Xaa is T or M

<220>
<221> misc_feature
<222> (275)..(275)
<223> Xaa is K or E

<400> 40

Gly Ser His Ser Met Arg Tyr Phe Ser Ala Ala Val Xaa Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Met Gly Xaa Val Asp Asp Xaa Gln
20 25 30

Phe Xaa Arg Phe Asp Ser Asp Ser Ala Cys Pro Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Xaa Glu Gly Pro Glu Tyr Trp Glu Glu Glu Thr
50 55 60

Arg Asn Thr Lys Ala His Ala Gln Thr Asp Arg Met Asn Leu Gln Thr
65 70 75 80

Xaa Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Ser Ser His Thr Leu Gln
85 90 95

Trp Met Ile Xaa Cys Asp Leu Xaa Xaa Asp Gly Arg Leu Xaa Arg Gly
100 105 110

Tyr Glu Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Leu Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Ser Lys
130 135 140

Arg Lys Cys Glu Ala Ala Asn Val Ala Glu Gln Arg Arg Ala Xaa Leu
145 150 155 160

```
Glu Gly Thr Cys Val Glu Trp Leu Xaa Arg Xaa Leu Glu Asn Gly Lys
                165                 170                 175

Glu Xaa Leu Gln Arg Ala Asp Pro Xaa Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Phe Asp Tyr Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Ile Leu Thr Trp Gln Xaa Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Val Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Xaa Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Met Leu
            260                 265                 270

Arg Trp Xaa Gln Ser Ser Leu Pro Thr Ile Pro Ile
        275                 280
```

<210> 41
<211> 275
<212> PRT
<213> Homo sapiens

<400> 41

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Lys Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60
```

```
Arg Asn Met Lys Ala His Ser Gln Thr Asp Arg Ala Asn Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Val His Ala Ala Glu Gln Arg Arg Val Tyr Leu
145                 150                 155                 160

Glu Gly Arg Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270
```

Arg Trp Glu
275

<210> 42
<211> 275
<212> PRT
<213> Homo sapiens

<400> 42

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
130 135 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145 150 155 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

```
Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 43
<211> 275
<212> PRT
<213> Homo sapiens

<400> 43

```
Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80
```

```
Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
            260                 265                 270

Ser Trp Glu
        275
```

<210> 44
<211> 276
<212> PRT
<213> Homo sapiens

<400> 44

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                  10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60


Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140


His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190
```

```
Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205


Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220


Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  45
<211>  274
<212>  PRT
<213>  Mus musculus

<400>  45

Gly Pro His Ser Leu Arg Tyr Phe Val Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15


Leu Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Asp Asn Pro Arg Phe Glu Pro Arg
        35                  40                  45


Ala Pro Trp Met Glu Gln Glu Gly Pro Glu Tyr Trp Glu Glu Gln Thr
    50                  55                  60


Gln Arg Ala Lys Ser Asp Glu Gln Trp Phe Arg Val Ser Leu Arg Thr
65                  70                  75                  80


Ala Gln Arg Tyr Tyr Asn Gln Ser Lys Gly Gly Ser His Thr Phe Gln
                85                  90                  95
```

```
Arg Met Phe Gly Cys Asp Val Gly Ser Asp Trp Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Gln Gln Phe Ala Tyr Asp Gly Arg Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Lys Thr Trp Thr Ala Ala Asp Thr Ala Ala Leu Ile Thr Arg
    130                 135                 140

Arg Lys Trp Glu Gln Ala Gly Asp Ala Glu Tyr Tyr Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Leu Gly Asn
                165                 170                 175

Glu Thr Leu Leu Arg Thr Asp Ser Pro Lys Ala His Val Thr Tyr His
            180                 185                 190

Pro Arg Ser Gln Val Asp Val Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Asp Ile Thr Leu Thr Trp Gln Leu Asn Gly Glu Asp Leu
    210                 215                 220

Thr Gln Asp Met Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Leu Gly Lys Glu Gln Asn
                245                 250                 255

Tyr Thr Cys His Val His His Lys Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp
```

<210> 46
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 46

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                  10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60


Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140


His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190
```

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 47
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 47

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65 70 75 80

```
Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Cys Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 48
<211> 276

<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 48

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
100 105 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
130 135 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
180 185 190

```
Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 49
<211> 276
<212> PRT
<213> Homo sapiens

<400> 49

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60

Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
```

```
                85                  90                  95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Ala Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Arg Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Leu
        275


<210>  50
<211>  276
<212>  PRT
```

<213> Homo sapiens

<400> 50

```
Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60


Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140


Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190


Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205
```

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 51
<211> 276
<212> PRT
<213> Homo sapiens

<400> 51

Gly Ser His Ser Met Arg Tyr Phe Thr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Arg Asn Val Lys Ala His Ser Gln Ile Asp Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Ile Gln
85 90 95

Met Met Tyr Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly

```
            100                 105                 110

Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 52
<211> 219
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (8)..(8)
<223> any amino acid other than aspartic acid

<400> 52

```
Phe Thr Val Thr Val Pro Lys Xaa Leu Tyr Val Val Glu Tyr Gly Ser
1               5                   10                  15


Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
            20                  25                  30


Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
        35                  40                  45


Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
    50                  55                  60


Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65                  70                  75                  80


Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
                85                  90                  95


Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
            100                 105                 110


Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
        115                 120                 125


Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
    130                 135                 140


Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145                 150                 155                 160


Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
                165                 170                 175


Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
```

180 185 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
195 200 205

Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
210 215

<210> 53
<211> 219
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (36)..(36)
<223> any amino acid other than isoleucine

<400> 53

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
1 5 10 15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
20 25 30

Ala Ala Leu Xaa Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
35 40 45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
50 55 60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65 70 75 80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
85 90 95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
100 105 110

```
Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
        115                 120                 125


Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
    130                 135                 140


Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145                 150                 155                 160


Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
                165                 170                 175


Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
            180                 185                 190


Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
        195                 200                 205


Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
    210                 215


<210>  54
<211>  219
<212>  PRT
<213>  Artificial sequence

<220>
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<220>
<221>  misc_feature
<222>  (54)..(54)
<223>  any amino acid other than glutamine

<400>  54

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
1               5                   10                  15


Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
            20                  25                  30


Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
```

```
        35                  40                  45

Phe Val His Gly Glu Xaa Asp Leu Lys Val Gln His Ser Ser Tyr Arg
    50                  55                  60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65                  70                  75                  80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
                85                  90                  95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
            100                 105                 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
        115                 120                 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
    130                 135                 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145                 150                 155                 160

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
                165                 170                 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
            180                 185                 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
        195                 200                 205

Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
    210                 215


<210>  55
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence
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<220>
<221> misc_feature
<222> (19)..(19)
<223> any amino acid other than asparagine

<400> 55

```
Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15


Gly His Xaa Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30


Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45


Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60


Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80


Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95


Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110


Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125


Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140


Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160


Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175


Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
```

180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 56
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (63)..(63)
<223> any amino acid other than asparagine

<400> 56

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Xaa Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

```
Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205
```

<210> 57
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (67)..(67)
<223> any amino acid other than isoleucine

<400> 57

```
Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60

Leu Ser Xaa Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
```

65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 58
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (86)..(86)
<223> any amino acid other than lysine

<400> 58

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

```
Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80

Glu Cys Val Val Leu Xaa Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205
```

<210> 59
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (4)..(4)
<223> any amino acid other than proline

<400> 59

Val Pro Gly Xaa Gly
1   5

<210> 60
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (157)..(157)
<223> any amino acid other than glutamine

<400> 60

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1   5   10   15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20   25   30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35   40   45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50   55   60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65   70   75   80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85   90   95

```
Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110


Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125


Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140


Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Xaa Asp Pro Glu
145                 150                 155                 160


Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175


Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190


Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  61
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (158)..(158)
<223>  any amino acid other than aspartic acid

<400>  61

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15


Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30


Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
```

```
        35                  40                  45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Xaa Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  62
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
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<222> (25)..(25)
<223> any amino acid other than leucine

<400> 62

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1   5   10   15

Gly His Asn Val Ser Val Glu Glu Xaa Ala Gln Thr Arg Ile Tyr Trp
            20   25   30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35   40   45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50   55   60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65   70   75   80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85   90   95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100   105   110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115   120   125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130   135   140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145   150   155   160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165   170   175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180   185   190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn

195 200 205

<210> 63
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (31)..(31)
<223> any amino acid other than tyrosine

<400> 63

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Xaa Trp
20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
130 135 140

```
Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160


Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175


Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190


Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  64
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (33)..(33)
<223>  any amino acid other than glutamine

<400>  64

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15


Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30


Xaa Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45


Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60


Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80


Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
```

```
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  65
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (38)..(38)
<223>  any amino acid other than methionine

<400>  65

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30
```

```
Gln Lys Glu Lys Lys Xaa Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205
```

<210> 66
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (39)..(39)
<223> any amino acid other than valine

<400> 66

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
20 25 30

Gln Lys Glu Lys Lys Met Xaa Leu Thr Met Met Ser Gly Asp Met Asn
35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
180 185 190

```
Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  67
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (49)..(49)
<223>  any amino acid other than isoleucine

<400>  67

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15


Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20                  25                  30


Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45


Xaa Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50                  55                  60


Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80


Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95


Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110


Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125


Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
```

130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 68
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (53)..(53)
<223> any amino acid other than tyrosine

<400> 68

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
35 40 45

Ile Trp Pro Glu Xaa Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

```
Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205
```

<210> 69
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (60)..(60)
<223> any amino acid other than aspartic acid

<400> 69

```
Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1               5                   10                  15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
```

```
            20                  25                  30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35                  40                  45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Xaa Ile Thr Asn Asn
    50                  55                  60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65                  70                  75                  80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85                  90                  95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
            100                 105                 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115                 120                 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130                 135                 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145                 150                 155                 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165                 170                 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180                 185                 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195                 200                 205


<210>  70
<211>  208
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence
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<220>
<221> misc_feature
<222> (108)..(108)
<223> any amino acid other than phenylalanine

<400> 70

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1   5   10   15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20   25   30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35   40   45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50   55   60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65   70   75   80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
                85   90   95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Xaa Pro Thr Pro Ser
            100   105   110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
        115   120   125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130   135   140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145   150   155   160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165   170   175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn

180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 71
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (156)..(156)
<223> any amino acid other than serine

<400> 71

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1 5 10 15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
20 25 30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
35 40 45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
50 55 60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr
65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Pro Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
    130   135   140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Xaa Gln Asp Pro Glu
145   150   155   160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
                165   170   175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
            180   185   190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
        195   200   205

<210> 72
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (111)..(111)
<223> any amino acid other than proline

<400> 72

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys
1   5   10   15

Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile Tyr Trp
            20   25   30

Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp Met Asn
        35   40   45

Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr Asn Asn
    50   55   60

Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly Thr Tyr

65 70 75 80

Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg Glu His
85 90 95

Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr Xaa Ser
100 105 110

Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile Ile Cys
115 120 125

Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu Glu Asn
130 135 140

Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp Pro Glu
145 150 155 160

Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met Thr Thr
165 170 175

Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg Val Asn
180 185 190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 73
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<400> 73

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

```
Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220
```

<210> 74

<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (66)..(66)
<223> any amino acid other than aspartic acid

<400> 74

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
100 105 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
115 120 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
130 135 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145 150 155 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
165 170 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
180 185 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
195 200 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
210 215 220

<210> 75
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (70)..(70)
<223> any amino acid other than tryptophan

<400> 75

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Xaa Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly

```
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220


<210>  76
<211>  224
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (91)..(91)
<223>  any amino acid other than histidine

<400>  76

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15
```

```
Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220
```

<210> 77

<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<400> 77

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 78
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature

<222> (66)..(66)
<223> any amino acid other than aspartic acid

<400> 78

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1   5   10   15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20   25   30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35   40   45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50   55   60

Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65   70   75   80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85   90   95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100   105   110

<210> 79
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (70)..(70)
<223> any amino acid other than tryptophan

<400> 79

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1   5   10   15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val

```
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Xaa Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100                 105                 110
```

<210> 80
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 80

```
Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60
```

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 81
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (41)..(41)
<223> any amino acid other than valine

<400> 81

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Xaa Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn

```
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220


<210>  82
<211>  110
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (41)..(41)
<223>  any amino acid other than valine

<400>  82

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30
```

```
Phe Trp Gln Asp Gln Glu Asn Leu Xaa Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100                 105                 110
```

<210> 83
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (35)..(35)
<223> any amino acid other than glutamine

<400> 83

```
Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Xaa Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
```

65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
100 105 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
115 120 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
130 135 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145 150 155 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
165 170 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
180 185 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
195 200 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
210 215 220

<210> 84
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (35)..(35)
<223> any amino acid other than glutamine

<400> 84

```
Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15


Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30


Phe Trp Xaa Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45


Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60


Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80


Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95


Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100                 105                 110
```

<210> 85
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (33)..(33)
<223> any amino acid other than phenylalanine

<400> 85

```
Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15


Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30


Xaa Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
```

```
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220
```

<210> 86
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (33)..(33)
<223> any amino acid other than phenylalanine

<400> 86

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Xaa Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 87
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (72)..(72)
<223> any amino acid other than leucine

<400> 87

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro

```
1               5                   10                  15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
    50                  55                  60

Phe Asp Ser Asp Ser Trp Thr Xaa Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220
```

<210> 88
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (72)..(72)
<223> any amino acid other than leucine

<400> 88

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Xaa Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 89
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (59)..(59)
<223> any amino acid other than tyrosine

<400> 89

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Xaa Met Asn Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
100 105 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
115 120 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
130 135 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145 150 155 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
165 170 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
180 185 190

```
Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205


Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220


<210>  90
<211>  110
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (59)..(59)
<223>  any amino acid other than tyrosine

<400>  90

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15


Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30


Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45


Lys Glu Lys Phe Asp Ser Val His Ser Lys Xaa Met Asn Arg Thr Ser
    50                  55                  60


Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80


Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr Gly
                85                  90                  95


Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100                 105                 110


<210>  91
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<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<220>
<221> misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 91

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
100 105 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
115 120 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
130 135 140

```
Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160


Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175


Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190


Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205


Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220


<210>  92
<211>  110
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (61)..(61)
<223>  any amino acid other than asparagine

<220>
<221>  misc_feature
<222>  (91)..(91)
<223>  any amino acid other than histidine

<400>  92

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1               5                   10                  15


Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
            20                  25                  30


Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
        35                  40                  45
```

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
50 55 60

Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 93
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (66)..(66)
<223> any amino acid other than aspartic acid

<220>
<221> misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 93

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

```
Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65                  70                  75                  80


Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
                85                  90                  95


Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
            100                 105                 110


Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
        115                 120                 125


Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
    130                 135                 140


Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145                 150                 155                 160


Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
                165                 170                 175


Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
            180                 185                 190


Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
        195                 200                 205


Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
    210                 215                 220


<210>  94
<211>  110
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (66)..(66)
<223>  any amino acid other than asparagine
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<220>
<221> misc_feature
<222> (91)..(91)
<223> Xaa can be any amino acid other than His

<400> 94

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Asn Arg Thr Ser
50 55 60

Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
100 105 110

<210> 95
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<220>
<221> Misc_feature
<222> (66)..(66)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 95

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
50 55 60

Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
85 90 95

Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala Asn
100 105 110

Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn Val
115 120 125

Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro Lys
130 135 140

Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr Asp
145 150 155 160

Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp Val
165 170 175

Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met Thr
180 185 190

Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser Pro
195 200 205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
210 215 220

<210> 96
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<220>
<221> Misc_feature
<222> (66)..(66)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 96

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro
1 5 10 15

Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val Val
20 25 30

Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu Gly
35 40 45

Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Xaa Arg Thr Ser
50 55 60

Phe Xaa Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile Lys
65 70 75 80

```
Asp Lys Gly Leu Tyr Gln Cys Ile Ile His Xaa Lys Lys Pro Thr Gly
                85                  90                  95


Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu
            100                 105                 110


<210>  97
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (47)..(47)
<223>  any amino acid other than lysine

<400>  97

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Xaa Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 98
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (147)..(147)
<223> any amino acid other than glutamine

<400> 98

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Xaa Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 99
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (11)..(11)
<223> any amino acid other than methionine

<400> 99

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Xaa Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 100
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (12)..(12)
<223> any amino acid other than phenylalanine

<400> 100

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Xaa Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 101
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (14)..(14)
<223> any amino acid other than glutamine

<400> 101

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Xaa Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 102
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (15)..(15)
<223> any amino acid other than leucine

<400> 102

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Xaa Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 103
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (16)..(16)
<223> any amino acid other than valine

<400> 103

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Xaa
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 104
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (18)..(18)
<223> any amino acid other than glutamine

<400> 104

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Xaa Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 105
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (19)..(19)
<223> any amino acid other than asparagined

<400> 105

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Xaa Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  106
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (20)..(20)
<223>  any amino acid other than valine

<400>  106

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Xaa Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 107
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (21)..(21)
<223> any amino acid other than leucine

<400> 107

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Xaa Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 108
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (22)..(22)
<223> any amino acid other than leucine

<400> 108

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Xaa Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 109
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (23)..(23)
<223> any amino acid other than isoleucine

<400> 109

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Xaa Asp Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 110
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (24)..(24)
<223> any amino acid other than aspartic acid

<400> 110

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Xaa Gly Pro Leu Ser Trp Tyr Ser Asp
```

20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 111
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (25)..(25)
<223> any amino acid other than glycine

<400> 111

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Asp Xaa Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 112
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (26)..(26)
<223> any amino acid other than proline

<400> 112

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Xaa Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 113
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (27)..(27)
<223> any amino acid other than leucine

<400> 113

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Xaa Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 114
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (28)..(28)
<223> any amino acid other than serine

<400> 114

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Xaa Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  115
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (29)..(29)
<223>  any amino acid other than tryptophan

<400>  115

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Xaa Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

```
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 116
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (30)..(30)
<223> any amino acid other than tyrosine

<400> 116

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Xaa Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95
```

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 117
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (31)..(31)
<223> any amino acid other than serine

<400> 117

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Xaa Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 118
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (32)..(32)
<223> any amino acid other than aspartic acid

<400> 118

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Xaa
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50   55   60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65   70   75   80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85   90   95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100   105   110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115   120   125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130   135   140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145   150   155   160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165   170

<210> 119
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (33)..(33)
<223> any amino acid other than proline

<400> 119

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1   5   10   15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp

20 25 30

Xaa Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 120
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (34)..(34)
<223> any amino acid other than glycine

<400> 120

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Xaa Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 121
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (35)..(35)
<223> any amino acid other than leucine

<400> 121

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Xaa Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125


Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140


Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 122
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (37)..(37)
<223> any amino acid other than glycine

<400> 122

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Xaa Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 123
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (38)..(38)
<223> any amino acid other than valine

<400> 123

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Xaa Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 124
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (39)..(39)
<223> any amino acid other than serine

<400> 124

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Xaa Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala

```
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 125
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (40)..(40)
<223> any amino acid other than leucine

<400> 125

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Xaa Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95
```

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 126
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (41)..(41)
<223> any amino acid other than threonine

<400> 126

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Xaa Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 127
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (42)..(42)
<223> any amino acid other than glycine

<400> 127

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Xaa Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 128
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (43)..(43)
<223> any amino acid other than glycine

<400> 128

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Xaa Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 129
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (44)..(44)
<223> any amino acid other than leucine

<400> 129

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Xaa Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 130
<211> 174
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> misc_feature
<222> (45)..(45)
<223> any amino acid other than serine

<400> 130

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Xaa Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 131
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (46)..(46)
<223> any amino acid other than tyrosine

<400> 131

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Xaa Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 132
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (48)..(48)
<223> any amino acid other than glutamic acid

<400> 132

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Xaa
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  133
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (49)..(49)
<223>  any amino acid other than aspartic acid

<400>  133

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Xaa Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

```
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 134
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (50)..(50)
<223> any amino acid other than threonine

<400> 134

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Xaa Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95
```

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 135
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (51)..(51)
<223> any amino acid other than lysine

<400> 135

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Xaa Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 136
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (52)..(52)
<223> any amino acid other than glutamic acid

<400> 136

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Xaa Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 137
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (64)..(64)
<223> any amino acid other than phenylalanine

<400> 137

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Xaa
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 138
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (65)..(65)
<223> any amino acid other than phenylalanine

<400> 138

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Xaa Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 139
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (66)..(66)
<223> any amino acid other than glutamine

<400> 139

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Xaa Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 140
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (67)..(67)
<223> any amino acid other than leucine

<400> 140

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Xaa Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 141
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (68)..(68)
<223> any amino acid other than glutamic acid

<400> 141

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Xaa Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  142
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (69)..(69)
<223>  any amino acid other than leucine

<400>  142

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Xaa Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

```
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 143
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (70)..(70)
<223> any amino acid other than arginine

<400> 143

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Xaa Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95
```

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 144
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (71)..(71)
<223> any amino acid other than arginine

<400> 144

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Xaa Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 145
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (72)..(72)
<223> any amino acid other than valine

<400> 145

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Xaa Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 146
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (73)..(73)
<223> any amino acid other than valine

<400> 146

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Xaa Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 147
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (75)..(75)
<223> any amino acid other than glycine

<400> 147

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Xaa Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 148
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (76)..(76)
<223> any amino acid other than glutamic acid

<400> 148

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Xaa Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 149
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (77)..(77)
<223> any amino acid other than glycine

<400> 149

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Xaa Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 150
<211> 174
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> misc_feature
<222> (78)..(78)
<223> any amino acid other than serine

<400> 150

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Xaa Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 151
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (104)..(104)
<223> any amino acid other than aspartic acid

<400> 151

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Xaa Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala

115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 152
<211> 174
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> misc_feature
<222> (105)..(105)
<223> any amino acid other than leucine

<400> 152

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

```
Ala Ala Leu Ala Leu Thr Val Asp Xaa Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
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<210> 153
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (106)..(106)
<223> any amino acid other than proline

<400> 153

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Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Xaa Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 154
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (109)..(109)
<223> any amino acid other than serine

<400> 154

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Xaa Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 155
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (110)..(110)
<223> any amino acid other than serine

<400> 155

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Xaa Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 156
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (111)..(111)
<223> any amino acid other than glutamic acid

<400> 156

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Xaa Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 157
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (113)..(113)
<223> any amino acid other than arginine

<400> 157

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Xaa Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 158
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (114)..(114)
<223> any amino acid other than asparagine

<400> 158

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Xaa Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 159
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (115)..(115)
<223> any amino acid other than serine

<400> 159

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Xaa Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  160
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (117)..(117)
<223>  any amino acid other than phenylalanine

<400>  160

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Xaa Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

```
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 161
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (130)..(130)
<223> any amino acid other than glutamine

<400> 161

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95
```

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Xaa Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 162
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (131)..(131)
<223> any amino acid other than arginine

<400> 162

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Xaa Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 163
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (132)..(132)
<223> any amino acid other than leucine

<400> 163

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Xaa Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 164
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (133)..(133)
<223> any amino acid other than glycine

<400> 164

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Xaa Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 165
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (134)..(134)
<223> any amino acid other than valine

<400> 165

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Xaa His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 166
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (135)..(135)
<223> any amino acid other than histidine

<400> 166

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val Xaa Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 167
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (136)..(136)
<223> any amino acid other than leucine

<400> 167

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Xaa His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 168
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (137)..(137)
<223> any amino acid other than histidine

<400> 168

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu Xaa Thr Glu Ala Arg Ala Arg His
130 135 140

```
Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160


Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170


<210>  169
<211>  174
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (138)..(138)
<223>  any amino acid other than threonine

<400>  169

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15


Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30


Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45


Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60


Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80


Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95


Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110


Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
```

115 120 125

Gly Gln Arg Leu Gly Val His Leu His Xaa Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 170
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (139)..(139)
<223> any amino acid other than glutamic acid

<400> 170

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Xaa Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 171
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (141)..(141)
<223> any amino acid other than arginine

<400> 171

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Xaa Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 172
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (143)..(143)
<223> any amino acid other than arginine

<400> 172

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

```
Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Xaa His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 173
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (144)..(144)
<223> any amino acid other than histidine

<400> 173

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
```

```
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg Xaa
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 174
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (146)..(146)
<223> any amino acid other than tryptophan

<400> 174

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                  10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65                  70                  75                  80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                85                  90                  95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Xaa Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 175
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (148)..(148)
<223> any amino acid other than leucine

<400> 175

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Xaa Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 176
<211> 174
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (149)..(149)
<223> any amino acid other than threonine

<400> 176

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Xaa Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu

165 170

<210> 177
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (150)..(150)
<223> any amino acid other than glutamine

<400> 177

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Xaa Gly Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 178
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (151)..(151)
<223> any amino acid other than glycine

<400> 178

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala

115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Xaa Ala Thr Val Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 179
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (153)..(153)
<223> any amino acid other than threonine

<400> 179

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
20 25 30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

```
Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            100                 105                 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        115                 120                 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    130                 135                 140

Ala Trp Gln Leu Thr Gln Gly Ala Xaa Val Leu Gly Leu Phe Arg Val
145                 150                 155                 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                165                 170
```

<210> 180
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (154)..(154)
<223> any amino acid other than valine

<400> 180

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1               5                   10                  15

Ala Gln Asn Val Leu Leu Ile Gly Gly Pro Leu Ser Trp Tyr Ser Asp
            20                  25                  30

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        35                  40                  45

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    50                  55                  60

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
```

65 70 75 80

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
85 90 95

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
130 135 140

Ala Trp Gln Leu Thr Gln Gly Ala Thr Xaa Leu Gly Leu Phe Arg Val
145 150 155 160

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 181
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<400> 181

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50   55   60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65   70   75   80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85   90   95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100   105   110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
        115   120   125

Ile Ser Thr Leu Thr
    130

<210> 182
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (20)..(20)
<223> any amino acid other than aspartic acid

<400> 182

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1   5   10   15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
            20   25   30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
        35   40   45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys

```
    50                  55                  60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65                  70                  75                  80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85                  90                  95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100                 105                 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
        115                 120                 125

Ile Ser Thr Leu Thr
    130


<210>  183
<211>  133
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (15)..(15)
<223>  any amino acid other than glutamic acid

<400>  183

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Xaa His
1               5                   10                  15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
            20                  25                  30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
        35                  40                  45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50                  55                  60
```

```
Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65                  70                  75                  80


Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85                  90                  95


Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100                 105                 110


Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
        115                 120                 125


Ile Ser Thr Leu Thr
    130


<210>  184
<211>  133
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence


<220>
<221>  misc_feature
<222>  (16)..(16)
<223>  any amino acid other than histidine

<400>  184

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1               5                   10                  15


Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
            20                  25                  30


Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
        35                  40                  45


Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50                  55                  60


Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
```

65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 185
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (16)..(16)
<223> any amino acid other than histidine

<400> 185

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 186
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine

<400> 186

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Xaa Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu

85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 187
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (126)..(126)
<223> any amino acid other than glutamine

<400> 187

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Xaa Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 188
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (16)..(16)
<223> any amino acid other than histidine

<220>
<221> misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<400> 188

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 189
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<400> 189

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu

65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 190
<211> 133
<212> PRT
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<220>
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<220>
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<222> (15)..(15)
<223> any amino acid other than glutamic aicd

<220>
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<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<400> 190

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Xaa His
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys

```
        35                  40                  45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50                  55                  60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65                  70                  75                  80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85                  90                  95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100                 105                 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
        115                 120                 125

Ile Ser Thr Leu Thr
    130


<210>  191
<211>  133
<212>  PRT
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<220>
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<220>
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<222>  (16)..(16)
<223>  any amino acid other than histidine

<220>
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<222>  (20)..(20)
<223>  any amino acid other than aspartic acid

<220>
<221>  Misc_feature
<222>  (42)..(42)
<223>  any amino acid other than phenylalanine

<400>  191

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
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1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 192
<211> 133
<212> PRT
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<220>
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<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (126)..(126)
<223> any amino acid other than glutamine

<400> 192

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Xaa Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 193
<211> 133
<212> PRT
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<220>
<223> synthetic sequence

<220>
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<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine

<400> 193

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Xaa Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 194
<211> 133
<212> PRT

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<220>
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<222> (16)..(16)
<223> any amino acid other than histidine

<220>
<221> Misc_feature
<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine

<400> 194

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Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1               5                   10                  15


Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
            20                  25                  30


Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Xaa Met Pro Lys
        35                  40                  45


Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
    50                  55                  60


Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65                  70                  75                  80


Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
                85                  90                  95


Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
            100                 105                 110
```

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 195
<211> 133
<212> PRT
<213> Artificial sequence

<220>
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<220>
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<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine

<220>
<221> Misc_feature
<222> (126)..(126)
<223> any amino acid other than glutamine

<400> 195

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Xaa Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys

50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Xaa Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 196
<211> 133
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> Misc_feature
<222> (16)..(16)
<223> any amino acid other than histidine

<220>
<221> Misc_feature
<222> (20)..(20)
<223> any amino acid other than aspartic acid

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine

<220>
<221> Misc_feature

<222> (126)..(126)
<223> any amino acid other than glutamine

<400> 196

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1 5 10 15

Leu Leu Leu Xaa Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Xaa Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Xaa Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 197
<211> 133
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> Misc_feature
<222> (16)..(16)
<223> any amino acid other than histidine

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>
<221> Misc_feature
<222> (126)..(126)
<223> any amino acid other than glutamine

<400> 197

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Xaa Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Xaa Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 198
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 198

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Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Lys Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60


Arg Asn Met Lys Ala His Ser Gln Thr Asp Arg Ala Asn Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95


Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140


Arg Lys Trp Glu Ala Val His Ala Ala Glu Gln Arg Arg Val Tyr Leu
145                 150                 155                 160


Glu Gly Arg Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190


Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
```

195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Leu
275

<210> 199
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 199

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln

```
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
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<210> 200
<211> 276
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 200

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                  10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60


Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Ile Gln
                85                  90                  95


Ile Met Tyr Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140


Arg Lys Trp Glu Ala Ala His Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Asp Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190
```

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Leu
275

<210> 201
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 201

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
50 55 60

Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65 70 75 80

```
Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Ala Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Arg Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Leu
        275
```

<210> 202

<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 202

```
Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60


Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
```

```
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  203
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  203

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60

Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
```

```
65                  70                  75                  80

Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
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<210> 204
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 204

```
Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60


Gly Lys Val Lys Ala Gln Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140


Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175
```

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
180 185 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 205
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 205

Gly Ser His Ser Met Arg Tyr Phe Thr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

```
Arg Asn Val Lys Ala His Ser Gln Ile Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Ile Gln
                85                  90                  95

Met Met Tyr Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
```

275

<210> 206
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 206

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Arg Lys Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
100 105 110

Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
130 135 140

Arg Lys Trp Glu Thr Ala His Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys

```
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 207
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 207

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
```

```
    50                  55                  60

Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270
```

Arg Trp Glu Pro
275

<210> 208
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 208

Gly Ser His Ser Met Arg Tyr Phe Asp Thr Ala Met Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Gln Ile Phe Lys Thr Asn Thr Gln Thr Asp Arg Glu Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

His Asn Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
130 135 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Asp Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Asp Thr Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
180 185 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 209
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 209

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Met Ala Pro Arg
35 40 45

```
Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Ser Lys Thr Asn Thr Gln Thr Tyr Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
```

260 265 270

Arg Trp Glu Pro
275

<210> 210
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 210

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Gln Ile Cys Lys Thr Asn Thr Gln Thr Tyr Arg Glu Asn Leu Arg Thr
65 70 75 80

Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

His Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
130 135 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Thr Tyr Leu

145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
180 185 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 211
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 211

Gly Ser His Ser Met Arg Tyr Phe His Thr Ala Met Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Thr Val Gly Tyr Val Asp Asp Thr Leu
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Thr Ser Pro Arg Lys Glu Pro Arg

```
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Ile Ser Lys Thr Asn Thr Gln Thr Tyr Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asn Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Ser Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255
```

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 212
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 212

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Met Ala Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
130 135 140

```
Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190


Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205


Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220


Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  213
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  213

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30
```

```
Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Thr Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Phe Lys Thr Asn Thr Gln Thr Tyr Arg Glu Asn Leu Arg Ile
65                  70                  75                  80

Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
```

245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 214
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 214

Cys Ser His Ser Met Lys Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Trp Met Cys Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln

```
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Met Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  215
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  215

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
```

```
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Arg Ser His Ile Ile Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240
```

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 216
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 216

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  217
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  217

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Trp Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Glu Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Asn Leu Arg Lys
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Phe Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
```

225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
260 265 270

Arg Trp Lys Pro
275

<210> 218
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 218

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Asn Leu Arg Lys
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
85 90 95

Trp Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu

```
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  219
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  219

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
```

```
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
260 265 270

Ser Trp Glu Pro
275

<210> 220
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 220

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
85 90 95

Arg Met Ser Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

```
Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
            260                 265                 270

Ser Trp Glu Pro
        275
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<400> 221

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Cys Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1               5                  10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Gln Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Thr Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Lys Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
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210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
260 265 270

Arg Trp Gly Pro
275

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<400> 222

Cys Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Asn Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Asn Leu Arg Lys
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
85 90 95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly

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            100                 105                 110

His Asp Gln Leu Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


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<400> 223

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 224

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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1   5   10

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<400> 226

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 227

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 228

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

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<400> 229

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

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<400> 230

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

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<400> 231

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 232

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 233

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 234

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 235

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 236

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1 5 10

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<400> 237

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

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<400> 238

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

<210> 239
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<400> 239

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1   5   10

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<400> 240

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 241

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 242

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 243

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

<210> 244
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<400> 244

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 245

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 246

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 247

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 248

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1   5   10

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<400> 249

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1   5   10

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<400> 250

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1   5   10

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<400> 251

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1   5   10

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 253

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 254

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 255

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1   5   10

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<400> 256

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 257

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 258

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1   5   10

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<400> 259

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 260

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<400> 261

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 262

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 263

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1 5 10

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<400> 264

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

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<400> 266

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 267

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 268

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

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<400> 269

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5   10

<210> 270
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<400> 270

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
1   5

<210> 272
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<220>
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<400> 272

Asp Tyr Lys Asp Asp Asp Asp Lys
1   5

<210> 273
<211> 10
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<400> 273

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1   5   10

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<211> 5
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<400> 274

His His His His His
1   5

<210> 275
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<220>
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<400> 275

His His His His His His
1   5

<210> 276
<211> 10
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<400> 276

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1 5 10

<210> 277
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<400> 277

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 278
<211> 8
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<400> 278

Trp Ser His Pro Gln Phe Glu Lys
1 5

<210> 279
<211> 9
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<220>
<223> synthetic sequence

<400> 279

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
1 5

<210> 280

<211> 5
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<220>
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<400> 280

Arg Tyr Ile Arg Ser
1 5

<210> 281
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<400> 281

Phe His His Thr
1

<210> 282
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<400> 282

Trp Glu Ala Ala Ala Arg Glu Ala Cys Cys Arg Glu Cys Cys Ala Arg
1 5 10 15

Ala

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<220>
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<400> 283

Ala Ala Ala Gly Gly
1 5

<210> 284
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<223> The residues at positions 1 to 4 may be repeated 1 to 10 times

<400> 284

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1 5

<210> 285
<211> 8
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<222> (1)..(8)
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<400> 285

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

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<400> 286

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 287
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 287

Gly Thr Leu Arg Gly
1   5

<210> 288
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 288

Tyr Asn Gln Ser Glu
1   5

<210> 289
<211> 5
<212> PRT
<213> Artificial sequence

<220>
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<400> 289

Thr Ala Ala Asp Met
1   5

<210> 290

<211> 5
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<400> 290

Ala Gln Thr Thr Lys
1   5

<210> 291
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<400> 291

Val Glu Thr Arg Pro
1   5

<210> 292
<211> 5
<212> PRT
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<220>
<223> synthetic sequence

<400> 292

Gly Asp Gly Thr Phe
1   5

<210> 293
<211> 5
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<220>
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<400> 293

Arg Asn Leu Arg Gly
1   5

<210> 294
<211> 5
<212> PRT
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<400> 294

Thr Ala Ala Asp Thr
1   5

<210> 295
<211> 5
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<400> 295

Ala Gln Ile Thr Gln
1   5

<210> 296
<211> 5
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<220>
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<400> 296

Gly Asp Arg Thr Phe
1   5

<210> 297
<211> 276
<212> PRT
<213> Homo sapiens

<400> 297

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1   5   10   15

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240
```

```
Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  298
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  298

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60


Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  299
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  299

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Cys Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

```
Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  300
<211>  275
<212>  PRT
<213>  Homo sapiens

<400>  300

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60


Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95


Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Ala Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 301
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 301

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60

Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Ala Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Ala Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
```

225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 302
<211> 341
<212> PRT
<213> Homo sapiens

<400> 302

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
50 55 60

Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65 70 75 80

Ala Leu Arg Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
100 105 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro Ser Ser Gln Pro Thr Val Pro Ile Val Gly Ile Ile
        275                 280                 285

Ala Gly Leu Val Leu Leu Gly Ala Val Ile Thr Gly Ala Val Val Ala
    290                 295                 300

Ala Val Met Trp Arg Arg Asn Ser Ser Asp Arg Lys Gly Gly Ser Tyr
305                 310                 315                 320

Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu
                325                 330                 335

Thr Ala Cys Lys Val
            340
```

<210> 303
<211> 341
<212> PRT
<213> Homo sapiens

<400> 303

```
Gly Ser His Ser Met Arg Tyr Phe Thr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60


Arg Asn Val Lys Ala His Ser Gln Ile Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Ile Gln
                85                  90                  95


Met Met Tyr Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
```

```
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro Ser Ser Gln Pro Thr Ile Pro Ile Val Gly Ile Ile
        275                 280                 285

Ala Gly Leu Val Leu Phe Gly Ala Val Phe Ala Gly Ala Val Val Ala
    290                 295                 300

Ala Val Arg Trp Arg Arg Lys Ser Ser Asp Arg Lys Gly Gly Ser Tyr
305                 310                 315                 320

Ser Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp Met Ser Leu
                325                 330                 335

Thr Ala Cys Lys Val
            340


<210>  304
<211>  276
<212>  PRT
<213>  Homo sapiens

<400>  304

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240
```

```
Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  305
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  305

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60


Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80


Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  306
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  306

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Cys Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

```
Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Arg Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  307
<211>  276
<212>  PRT
<213>  Homo sapiens

<400>  307

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45


Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
            260                 265                 270

Ser Trp Glu Pro
        275


<210>  308
<211>  276
<212>  PRT
<213>  Homo sapiens

<400>  308

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30
```

```
Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Ala Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240
```

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
260 265 270

Ser Trp Glu Pro
275

<210> 309
<211> 246
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (78)..(79)
<223> Amino acid cluster 1 is present between the residues at positions 78 and 79.

<220>
<221> MISC_FEATURE
<222> (79)..(79)
<223> The cysteine residue forms a disulfide bond between the alpha1 and alpha2-1 helices.

<220>
<221> MISC_FEATURE
<222> (79)..(80)
<223> Amino acid cluster 2 is present between the residues at positions 79 and 80.

<220>
<221> MISC_FEATURE
<222> (123)..(124)
<223> Amino acid cluster 3 is present between the residues at positions 123 and 124.

<220>
<221> MISC_FEATURE
<222> (124)..(124)
<223> The cysteine residue at position 124 forms a disulfide bond between the alpha1 and alpha2-1 helices

<220>
<221> MISC_FEATURE
<222> (124)..(125)

<223> Amino acid cluster 4 is present between the residues at positions 124 and 125.

<220>
<221> MISC_FEATURE
<222> (210)..(211)
<223> Amino acid cluster 5 is present between the residues at positions 210 and 211.

<220>
<221> MISC_FEATURE
<222> (211)..(211)
<223> The cysteine residue forms a disulfide bond with the beta2M polypeptide cysteine at position 12.

<220>
<221> MISC_FEATURE
<222> (211)..(212)
<223> Amino acid cluster 6 is present between the residues at positions 211 and 212.

<220>
<221> MISC_FEATURE
<222> (212)..(213)
<223> Amino acid cluster 6 is present between the residues at positions 211 and 212.

<400> 309

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Cys Ala
65 70 75 80

Gly Ser His Thr Val Gln Arg Met Tyr Gly Cys Asp Val Gly Ser Asp
85 90 95

Trp Arg Phe Leu Arg Gly Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp

```
            100                 105                 110

Tyr Ile Ala Leu Lys Glu Asp Leu Arg Ser Trp Cys His Lys Trp Glu
        115                 120                 125

Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys
    130                 135                 140

Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln
145                 150                 155                 160

Arg Thr Asp Ala Pro Lys Thr His Met Thr His His Ala Val Ser Asp
                165                 170                 175

His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe Tyr Pro Ala Glu
            180                 185                 190

Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr
        195                 200                 205

Glu Leu Cys Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu
    210                 215                 220

Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu
225                 230                 235                 240

Thr Leu Arg Trp Glu Pro
                245
```

<210> 310
<211> 99
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 310

```
Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu
1               5                   10                  15

Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
```

```
            20                  25                  30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
        35                  40                  45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
    50                  55                  60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65                  70                  75                  80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
                85                  90                  95

Arg Asp Met
```

<210> 311
<211> 99
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 311

```
Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Cys His Pro Ala Glu
1               5                   10                  15

Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
            20                  25                  30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
        35                  40                  45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
    50                  55                  60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65                  70                  75                  80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
```

85 90 95

Arg Asp Met

<210> 312
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 312

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
100 105 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
130 135 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu

145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
180 185 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu Pro
275

<210> 313
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 313

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg

```
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255
```

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 314
<211> 99
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 314

Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Cys His Pro Ala Glu
1 5 10 15

Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro
20 25 30

Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys
35 40 45

Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu
50 55 60

Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys
65 70 75 80

Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp
85 90 95

Arg Asp Met

<210> 315
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (6)..(10)
<223> The amino acids from positions 6 to 10 may be repeated 1, 2, 3,
       4, 5, 6, 7, 8, or 9 times

<400> 315

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10

<210> 316
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 316

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 317
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 317

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10   15

<210> 318
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 318

Gly Cys Gly Gly Ser
1 5

<210> 319
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (6)..(10)
<223> The amino acids at positions 6 to 10 may be repeated 1 to 10 times

<400> 319

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 320
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 320

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 321
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 321

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
            20

<210> 322
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 322

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
            20   25

<210> 323
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 323

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            20   25   30

<210> 324
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 324

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser
        35

<210> 325
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 325

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser
        35   40

<210> 326
<211> 45
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 326

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        35   40   45

<210> 327

<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 327

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser
50

<210> 328
<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 328

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 329
<211> 5
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 329

Cys Gly Gly Gly Ser
1 5

<210> 330
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (6)..(10)
<223> The amino acids at positions 6 to 10 can be repeated 1 to 10 times

<400> 330

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 331
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 331

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 332
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 332

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 333
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 333

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 334
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 334

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25

<210> 335
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 335

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            20   25   30

<210> 336
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 336

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser
        35

<210> 337
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 337

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser
        35   40

<210> 338
<211> 45
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 338

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        35   40   45

<210> 339
<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 339

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        35   40   45

Gly Ser
    50

<210> 340
<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 340

```
Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1               5                   10                  15


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20                  25                  30


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        35                  40                  45


Gly Ser Gly Gly Gly Gly Ser
    50                  55
```

<210> 341
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 341

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60


Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110
```

```
Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 342
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>

<221> MISC_FEATURE
<222> (6)..(10)
<223> The residues from positions 6 to 10 may be repeated 1 to 10 times

<400> 342

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 343
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 343

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Lys Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
50 55 60

Arg Asn Met Lys Ala His Ser Gln Thr Asp Arg Ala Asn Leu Gly Thr
65 70 75 80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
85 90 95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
100 105 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
130 135 140

```
Arg Lys Trp Glu Ala Val His Ala Ala Glu Gln Arg Arg Val Tyr Leu
145                 150                 155                 160

Glu Gly Arg Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275


<210>  344
<211>  275
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  344

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30
```

```
Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr
    50                  55                  60

Arg Asn Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
                85                  90                  95

Ile Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Ala Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Arg Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240
```

```
Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu
        275


<210>  345
<211>  275
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  345

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60


Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 346
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 346

```
Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60

Gly Lys Val Lys Ala His Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80

Ala Leu Arg Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240
```

```
Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu
        275


<210>  347
<211>  275
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  347

Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Glu Glu Thr
    50                  55                  60


Gly Lys Val Lys Ala Gln Ser Gln Thr Asp Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Met Met Phe Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125
```

```
Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys
    130                 135                 140

Arg Lys Trp Glu Ala Ala His Val Ala Glu Gln Gln Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 348
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 348

```
Gly Ser His Ser Met Arg Tyr Phe Thr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15
```

```
Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Arg Asn Val Lys Ala His Ser Gln Ile Asp Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Ile Gln
                85                  90                  95

Met Met Tyr Gly Cys Asp Val Gly Ser Asp Gly Arg Phe Leu Arg Gly
            100                 105                 110

Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 349
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 349

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
50 55 60

Arg Lys Val Lys Ala Gln Ser Gln Thr Asp Arg Val Asp Leu Gly Thr
65 70 75 80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln
85 90 95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly
100 105 110

```
Tyr Gln Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Thr Ala His Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ser Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 350
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 350

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Tyr Lys Ala Gln Ala Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

```
Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240


Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255


Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270


Arg Trp Glu Pro
        275


<210>  351
<211>  275
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  351

Gly Ser His Ser Met Arg Tyr Phe Asp Thr Ala Met Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60


Gln Ile Phe Lys Thr Asn Thr Gln Thr Asp Arg Glu Ser Leu Arg Asn
65                  70                  75                  80


Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Ser Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110
```

```
His Asn Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Asp Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Asp Thr Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 352
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 352

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1               5                  10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Met Ala Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Ser Lys Thr Asn Thr Gln Thr Tyr Arg Glu Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205
```

```
Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 353
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 353

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ser Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Glu Glu Pro Arg
        35                  40                  45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60

Gln Ile Cys Lys Thr Asn Thr Gln Thr Tyr Arg Glu Asn Leu Arg Thr
65                  70                  75                  80

Ala Leu Arg Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95
```

```
Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Thr Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 354
<211> 275
<212> PRT
<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 354

```
Gly Ser His Ser Met Arg Tyr Phe His Thr Ala Met Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Thr Val Gly Tyr Val Asp Asp Thr Leu
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Thr Ser Pro Arg Lys Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Gln Ile Ser Lys Thr Asn Thr Gln Thr Tyr Arg Glu Ser Leu Arg Asn
65                  70                  75                  80


Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


His Asn Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Ser Gln
    130                 135                 140


Arg Lys Leu Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Glu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Asp Lys Leu Glu Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190


Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205
```

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 355
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 355

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Met Ala Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

```
Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 356
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 356

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Met Ser Arg Pro Gly
1               5                  10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Thr Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Asn Thr
    50                  55                  60


Gln Ile Phe Lys Thr Asn Thr Gln Thr Tyr Arg Glu Asn Leu Arg Ile
65                  70                  75                  80


Ala Leu Arg Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


His Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Ser Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Trp Glu Ala Ala Arg Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175


Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Thr His Val Thr His His
            180                 185                 190
```

```
Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Arg Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
        275
```

<210> 357
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 357

```
Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80
```

```
Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
            260                 265                 270

Ser Trp Glu Pro
        275
```

<210> 358
<211> 276

<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 358

Cys Ser His Ser Met Lys Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
35 40 45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
50 55 60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65 70 75 80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
85 90 95

Trp Met Cys Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
100 105 110

Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
115 120 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
130 135 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145 150 155 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
165 170 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
180 185 190

```
Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Met Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275


<210>  359
<211>  276
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic sequence

<400>  359

Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80
```

```
Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Arg Ser His Ile Ile Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 360
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 360

```
Gly Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45


Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80


Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


Tyr Asp Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Leu Cys Val Glu Trp Leu Arg Arg Tyr Leu Lys Asn Gly Lys
                165                 170                 175
```

```
Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 361
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 361

```
Gly Ser His Ser Met Arg Tyr Phe Ser Thr Ser Val Ser Trp Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Glu Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60
```

```
Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Asn Leu Arg Lys
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Phe Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Arg Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Trp Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Lys Pro
        275
```

<210> 362
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 362

```
Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15


Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45


Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60


Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Asn Leu Arg Lys
65                  70                  75                  80


Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95


Trp Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110


Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140


Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Trp Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175
```

```
Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 363
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 363

```
Cys Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1               5                   10                  15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Gln Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60
```

```
Gln Lys Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asn Gln Phe Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Trp Glu Ala Ala Arg Thr Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Lys Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270
```

Arg Trp Gly Pro
        275

<210> 364
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 364

Cys Ser His Ser Met Arg Tyr Phe Tyr Thr Ala Val Ser Arg Pro Gly
1   5   10   15

Arg Gly Glu Pro His Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20   25   30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35   40   45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50   55   60

Gln Asn Tyr Lys Arg Gln Ala Gln Thr Asp Arg Val Asn Leu Arg Lys
65   70   75   80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Ala Gly Ser His Ile Ile Gln
                85   90   95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100   105   110

His Asp Gln Leu Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115   120   125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130   135   140

Arg Lys Trp Glu Ala Ala Arg Glu Ala Glu Gln Leu Arg Ala Tyr Leu
145   150   155   160

```
Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu His Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Glu Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu Pro
        275
```

<210> 365
<211> 223
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 365

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Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
1               5                   10                  15

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            20                  25                  30

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
        35                  40                  45
```

```
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    50                  55                  60

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
65                  70                  75                  80

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                85                  90                  95

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
            100                 105                 110

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        115                 120                 125

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
    130                 135                 140

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
145                 150                 155                 160

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                165                 170                 175

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
            180                 185                 190

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        195                 200                 205

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
    210                 215                 220
```

<210> 366
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>

<221> MISC_FEATURE
<222> (1)..(2)
<223> The amino acids from positions 1 to 2 may be repeated at least once

<220>
<221> MISC_FEATURE
<222> (3)..(7)
<223> The amino acids at positions 3 to 7 may be repeated at least once

<400> 366

Gly Ser Gly Ser Gly Gly Ser
1 5

<210> 367
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (1)..(4)
<223> The amino acids at positions 1 to 4 may be repeated at least once

<400> 367

Gly Gly Gly Ser
1

<210> 368
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 368

Gly Gly Ser Gly
1

<210> 369
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 369

Gly Gly Ser Gly Gly
1   5

<210> 370
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 370

Gly Ser Gly Ser Gly
1   5

<210> 371
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 371

Gly Ser Gly Gly Gly
1   5

<210> 372
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 372

Gly Gly Gly Ser Gly
1   5

<210> 373
<211> 5

<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 373

Gly Ser Ser Ser Gly
1 5

<210> 374
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 374

Gly Ser Ser Ser Ser
1 5

<210> 375
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 375

Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
1 5 10 15

Ser Ser Ser Ser
20

<210> 376
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 376

Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
1   5   10   15

Ser Ser Ser Ser Gly Ser Ser Ser Ser
            20   25

<210> 377
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 377

Gly Gly Gly Gly Ser
1   5

<210> 378
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 378

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10

<210> 379
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 379

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10   15

<210> 380
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 380

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser
            20

<210> 381
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 381

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
            20   25

<210> 382
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 382

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
            20   25   30

<210> 383
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 383

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser
        35

<210> 384
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 384

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser
        35   40

<210> 385
<211> 45
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 385

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        35   40   45

<210> 386
<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 386

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
            20   25   30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        35   40   45

Gly Ser
    50

<210> 387
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 387

Ala Ala Ala Gly Gly
1   5

<210> 388
<211> 8
<212> PRT
<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 388

Leu Glu Val Leu Phe Gln Gly Pro
1 5

<210> 389
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 389

Glu Asn Leu Tyr Thr Gln Ser
1 5

<210> 390
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 390

Asp Asp Asp Asp Lys
1 5

<210> 391
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 391

Leu Val Pro Arg
1

<210> 392
<211> 22
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 392

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1   5   10   15

Glu Glu Asn Pro Gly Pro
            20

<210> 393
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> MISC_FEATURE
<222> (6)..(10)
<223> The amino acids from positions 6 to 10 may be repeated 1, 2, or 3
       times.

<400> 393

Gly Cys Gly Gly Gly Gly Gly Gly Ser
1   5

<210> 394
<211> 6
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 394

Cys His Tyr Ser Glu Leu
1   5

<210> 395
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 395

Gly Ile Leu Gly Phe Val Phe Thr Leu
1   5

<210> 396
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 396

His Pro Val Gly Glu Ala Asp Tyr Phe
1   5

<210> 397
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 397

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1   5   10   15

Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20   25   30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35   40   45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50   55   60

Gln Asn Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65   70   75   80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln

```
                85                  90                  95

Arg Met Tyr Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Cys Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
            260                 265                 270

Ser Trp Glu Pro
        275

<210>  398
<211>  10
<212>  PRT
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<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 398

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 399
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 399

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 400
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 400

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 401
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)

<223> Xaa can be any naturally occurring amino acid

<400> 401

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 402
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 402

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 403
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 403

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 404
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 404

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1   5   10   15

```
Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Pro Arg Gly Glu Pro Arg
        35                  40                  45

Ala Pro Trp Val Glu Gln Glu Gly Pro Glu Tyr Trp Asp Arg Glu Thr
    50                  55                  60

Gln Lys Tyr Lys Arg Gln Ala Gln Ala Asp Arg Val Ser Leu Arg Asn
65                  70                  75                  80

Leu Arg Gly Cys Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Leu Gln
                85                  90                  95

Arg Met Ser Gly Cys Asp Leu Gly Pro Asp Gly Arg Leu Leu Arg Gly
            100                 105                 110

Tyr Asp Gln Ser Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Ala Ala Gln Ile Thr Gln
    130                 135                 140

Arg Lys Leu Glu Ala Ala Arg Ala Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Ala Glu Pro Pro Lys Thr His Val Thr His His
            180                 185                 190

Pro Leu Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220
```

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Met Gln His Glu Gly Leu Gln Glu Pro Leu Thr Leu
260 265 270

Ser Trp Glu Pro
275

<210> 405
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 405

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 406
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 406

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 407
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 407

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 408
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 408

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 409
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)

<223> Xaa can be any naturally occurring amino acid

<400> 409

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 410
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 410

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 411
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 411

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 412
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 412

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 413
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 413

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 414
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 414

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 415
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 415

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 416
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 416

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 417
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 417

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 418
<211> 7
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 418

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 419

<211> 7
<212> PRT
<213> Artificial sequence

<220>
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<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 419

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 420
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 420

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 421
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 421

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 422
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 422

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 423
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 423

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 424
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 424

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 425
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 425

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 426
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 426

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 427
<211> 7
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 427

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 428
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 428

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 429
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 429

Xaa Xaa Xaa Xaa Xaa Xaa Xaa

1 5

<210> 430
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 430

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 431
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 431

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 432
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature

<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 432

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 433
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 433

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 434
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 434

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 435
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 435

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 436
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 436

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 437
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 437

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 438
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 438

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 439
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 439

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 440
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 440

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 441
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 441

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 442
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 442

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 443
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 443

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 444
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 444

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 445
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 445

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 446

<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 446

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 447
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 447

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1   5

<210> 448
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> misc_feature
<222> (1)..(7)
<223> Xaa can be any naturally occurring amino acid

<400> 448

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 449
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 449

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

```
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175


Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190


Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205


His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220


Pro Gly Lys
225
```

<210> 450
<211> 325
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 450

```
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser
1               5                   10                  15


Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
            20                  25                  30


Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
        35                  40                  45


Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
    50                  55                  60


Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr
65                  70                  75                  80


Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr
                85                  90                  95
```

```
Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro
            100                 105                 110

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        115                 120                 125

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    130                 135                 140

Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
145                 150                 155                 160

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
                165                 170                 175

Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu
            180                 185                 190

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala
        195                 200                 205

Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro
    210                 215                 220

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
225                 230                 235                 240

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                245                 250                 255

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            260                 265                 270

Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
        275                 280                 285

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    290                 295                 300

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
```

305 310 315 320

Leu Ser Pro Gly Lys
325

<210> 451
<211> 246
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 451

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Leu Lys Thr
1 5 10 15

Pro Leu Gly Asp Thr Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
20 25 30

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
35 40 45

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
50 55 60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65 70 75 80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
85 90 95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
100 105 110

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
115 120 125

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
130 135 140

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn

145 150 155 160

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
165 170 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
180 185 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
210 215 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225 230 235 240

Ser Leu Ser Pro Gly Lys
245

<210> 452
<211> 383
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 452

Pro Thr Lys Ala Pro Asp Val Phe Pro Ile Ile Ser Gly Cys Arg His
1 5 10 15

Pro Lys Asp Asn Ser Pro Val Val Leu Ala Cys Leu Ile Thr Gly Tyr
20 25 30

His Pro Thr Ser Val Thr Val Thr Trp Tyr Met Gly Thr Gln Ser Gln
35 40 45

Pro Gln Arg Thr Phe Pro Glu Ile Gln Arg Arg Asp Ser Tyr Tyr Met
50 55 60

Thr Ser Ser Gln Leu Ser Thr Pro Leu Gln Gln Trp Arg Gln Gly Glu

```
65                  70                  75                  80

Tyr Lys Cys Val Val Gln His Thr Ala Ser Lys Ser Lys Lys Glu Ile
                85                  90                  95

Phe Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr
            100                 105                 110

Ala Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro
        115                 120                 125

Ala Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu
    130                 135                 140

Lys Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys
145                 150                 155                 160

Pro Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val
                165                 170                 175

Gln Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val
            180                 185                 190

Gly Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys
        195                 200                 205

Val Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn
    210                 215                 220

Gly Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp
225                 230                 235                 240

Asn Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro
                245                 250                 255

Pro Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val
            260                 265                 270

Lys Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala
        275                 280                 285
```

```
Ser Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu
    290                 295                 300

Leu Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala
305                 310                 315                 320

Pro Ala Arg Pro Pro Pro Gln Pro Arg Ser Thr Thr Phe Trp Ala Trp
                325                 330                 335

Ser Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr
            340                 345                 350

Thr Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser
        355                 360                 365

Arg Ser Leu Glu Val Ser Tyr Val Thr Asp His Gly Pro Met Lys
    370                 375                 380
```

<210> 453
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 453

```
Val Thr Ser Thr Leu Thr Ile Lys Glx Ser Asp Trp Leu Gly Glu Ser
1               5                   10                  15

Met Phe Thr Cys Arg Val Asp His Arg Gly Leu Thr Phe Gln Gln Asn
            20                  25                  30

Ala Ser Ser Met Cys Val Pro Asp Gln Asp Thr Ala Ile Arg Val Phe
        35                  40                  45

Ala Ile Pro Pro Ser Phe Ala Ser Ile Phe Leu Thr Lys Ser Thr Lys
    50                  55                  60

Leu Thr Cys Leu Val Thr Asp Leu Thr Thr Tyr Asx Ser Val Thr Ile
65                  70                  75                  80
```

```
Ser Trp Thr Arg Glu Glu Asn Gly Ala Val Lys Thr His Thr Asn Ile
                85                  90                  95

Ser Glu Ser His Pro Asn Ala Thr Phe Ser Ala Val Gly Glu Ala Ser
            100                 105                 110

Ile Cys Glu Asp Asx Asp Trp Ser Gly Glu Arg Phe Thr Cys Thr Val
        115                 120                 125

Thr His Thr Asp Leu Pro Ser Pro Leu Lys Gln Thr Ile Ser Arg Pro
    130                 135                 140

Lys Gly Val Ala Leu His Arg Pro Asx Val Tyr Leu Leu Pro Pro Ala
145                 150                 155                 160

Arg Glx Glx Leu Asn Leu Arg Glu Ser Ala Thr Ile Thr Cys Leu Val
                165                 170                 175

Thr Gly Phe Ser Pro Ala Asp Val Phe Val Glu Trp Met Gln Arg Gly
            180                 185                 190

Glu Pro Leu Ser Pro Gln Lys Tyr Val Thr Ser Ala Pro Met Pro Glu
        195                 200                 205

Pro Gln Ala Pro Gly Arg Tyr Phe Ala His Ser Ile Leu Thr Val Ser
    210                 215                 220

Glu Glu Glu Trp Asn Thr Gly Gly Thr Tyr Thr Cys Val Val Ala His
225                 230                 235                 240

Glu Ala Leu Pro Asn Arg Val Thr Glu Arg Thr Val Asp Lys Ser Thr
                245                 250                 255

Gly Lys Pro Thr Leu Tyr Asn Val Ser Leu Val Met Ser Asp Thr Ala
            260                 265                 270

Gly Thr Cys Tyr
        275
```

<210> 454

<211> 353
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 454

Ala Ser Pro Thr Ser Pro Lys Val Phe Pro Leu Ser Leu Cys Ser Thr
1 5 10 15

Gln Pro Asp Gly Asn Val Val Ile Ala Cys Leu Val Gln Gly Phe Phe
20 25 30

Pro Gln Glu Pro Leu Ser Val Thr Trp Ser Glu Ser Gly Gln Gly Val
35 40 45

Thr Ala Arg Asn Phe Pro Pro Ser Gln Asp Ala Ser Gly Asp Leu Tyr
50 55 60

Thr Thr Ser Ser Gln Leu Thr Leu Pro Ala Thr Gln Cys Leu Ala Gly
65 70 75 80

Lys Ser Val Thr Cys His Val Lys His Tyr Thr Asn Pro Ser Gln Asp
85 90 95

Val Thr Val Pro Cys Pro Val Pro Ser Thr Pro Pro Thr Pro Ser Pro
100 105 110

Ser Thr Pro Pro Thr Pro Ser Pro Ser Cys Cys His Pro Arg Leu Ser
115 120 125

Leu His Arg Pro Ala Leu Glu Asp Leu Leu Leu Gly Ser Glu Ala Asn
130 135 140

Leu Thr Cys Thr Leu Thr Gly Leu Arg Asp Ala Ser Gly Val Thr Phe
145 150 155 160

Thr Trp Thr Pro Ser Ser Gly Lys Ser Ala Val Gln Gly Pro Pro Glu
165 170 175

Arg Asp Leu Cys Gly Cys Tyr Ser Val Ser Ser Val Leu Pro Gly Cys

```
            180                 185                 190

Ala Glu Pro Trp Asn His Gly Lys Thr Phe Thr Cys Thr Ala Ala Tyr
        195                 200                 205

Pro Glu Ser Lys Thr Pro Leu Thr Ala Thr Leu Ser Lys Ser Gly Asn
    210                 215                 220

Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu Glu Leu
225                 230                 235                 240

Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly Phe Ser
                245                 250                 255

Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu Leu Pro
            260                 265                 270

Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser Gln Gly
        275                 280                 285

Thr Thr Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala Glu Asp
    290                 295                 300

Trp Lys Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu Ala Leu
305                 310                 315                 320

Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg Leu Ala Gly Lys Pro
                325                 330                 335

Thr His Val Asn Val Ser Val Val Met Ala Glu Val Asp Gly Thr Cys
            340                 345                 350

Tyr
```

<210> 455
<211> 222
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 455

```
Ala Asp Pro Cys Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser
1               5                  10                  15

Arg Pro Ser Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr Ile Thr
            20                  25                  30

Cys Leu Val Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn Leu Thr
        35                  40                  45

Trp Ser Arg Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg Lys Glu
    50                  55                  60

Glu Lys Gln Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu Pro Val
65                  70                  75                  80

Gly Thr Arg Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg Val Thr
                85                  90                  95

His Pro His Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys Thr Ser
            100                 105                 110

Gly Pro Arg Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro Glu Trp
        115                 120                 125

Pro Gly Ser Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln Asn Phe
    130                 135                 140

Met Pro Glu Asp Ile Ser Val Gln Trp Leu His Asn Glu Val Gln Leu
145                 150                 155                 160

Pro Asp Ala Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys Gly Ser
                165                 170                 175

Gly Phe Phe Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu Trp Glu
            180                 185                 190

Gln Lys Asp Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala Ser Pro
        195                 200                 205
```

Ser Gln Thr Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys
210 215 220

<210> 456
<211> 327
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 456

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

```
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                245                 250                 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            260                 265                 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        275                 280                 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
    290                 295                 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305                 310                 315                 320

Leu Ser Leu Ser Leu Gly Lys
                325
```

<210> 457
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 457

```
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1               5                  10                  15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
```

210 215 220

Pro Gly Lys
225

<210> 458
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 458

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu

145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 459
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 459

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly

```
                85                  90                  95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220

Pro Gly Lys
225
```

<210> 460
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 460

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
1               5                   10                  15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
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            20                  25                  30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220

Pro Gly Lys
225
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<210> 461
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequences

<400> 461

```
Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1               5                  10                  15


Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
            20                  25                  30


Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
        35                  40                  45


Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
    50                  55                  60


Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80


Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95


Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110


Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125


Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140


His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160


Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175
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Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
180 185 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
195 200 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
210 215 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr
225 230 235 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
245 250 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
260 265 270

Arg Trp Glu
275

<210> 462
<211> 275
<212> PRT
<213> Artificial sequence

<220>
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<400> 462

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

Arg Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln
20 25 30

Phe Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg
35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr
50 55 60

```
Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Gly Thr
65                  70                  75                  80

Leu Arg Gly Ala Tyr Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln
                85                  90                  95

Arg Met Tyr Gly Cys Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly
            100                 105                 110

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
        115                 120                 125

Asp Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys
    130                 135                 140

His Lys Trp Glu Ala Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu
145                 150                 155                 160

Glu Gly Thr Cys Val Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys
                165                 170                 175

Glu Thr Leu Gln Arg Thr Asp Ala Pro Lys Thr His Met Thr His His
            180                 185                 190

Ala Val Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe
        195                 200                 205

Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln
    210                 215                 220

Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Cys Gly Asp Gly Thr
225                 230                 235                 240

Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Gln Glu Gln Arg
                245                 250                 255

Tyr Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu
            260                 265                 270

Arg Trp Glu
```