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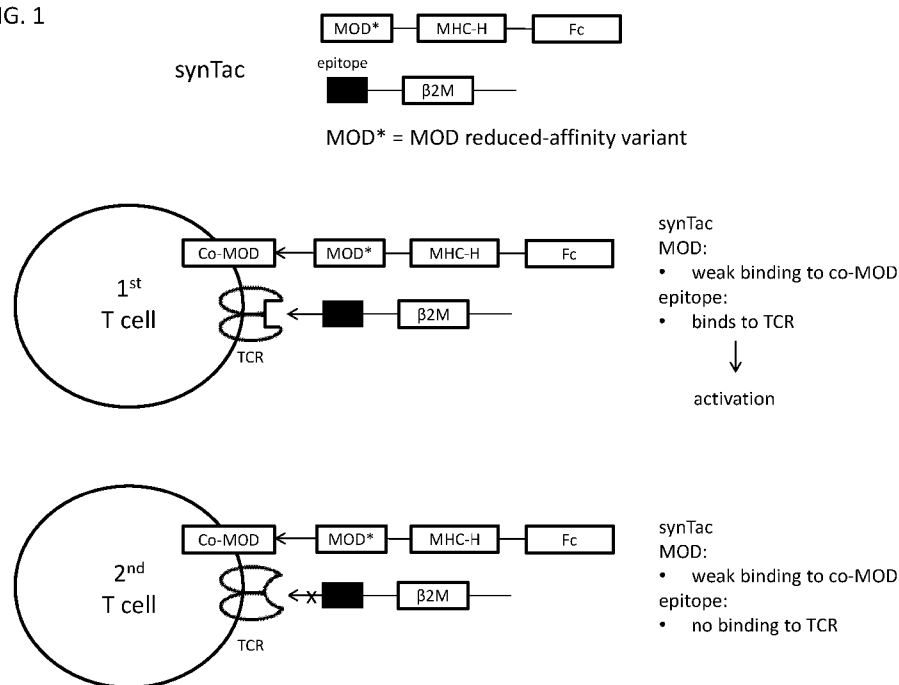
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(54) Title: MULTIMERIC T-CELL MODULATORY POLYPEPTIDES AND METHODS OF USE THEREOF

FIG. 1



(57) Abstract: The present disclosure provides T-cell modulatory multimeric polypeptides that comprise an immunomodulatory polypeptide that exhibits reduced binding affinity to a cognate co-immunomodulatory polypeptide. 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.

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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. 62/555,499, filed September 7, 2017, which application is incorporated herein by reference in its 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 that exhibits reduced binding affinity to a cognate co-immunomodulatory polypeptide. A TMMP is useful for modulating the activity of a T cell, and for modulating an immune response in an individual.
- [0003A]** The present disclosure provides a T-cell modulatory multimeric polypeptide (TMMP) comprising:
- at least one heterodimer comprising:
 - a) a first polypeptide comprising:
 - i) a Wilms tumor-1 (WT-1) peptide epitope, wherein the WT-1 peptide has a length of from 4 amino acids to 20 amino acids; and;

ii) a first class I major histocompatibility complex (MHC) polypeptide, wherein the first MHC polypeptide is a $\beta 2$ microglobulin ($\beta 2M$) polypeptide;
 b) a second polypeptide comprising a second class I MHC polypeptide, wherein the second class I MHC polypeptide is a class I MHC heavy chain polypeptide; and
 c) two immunomodulatory polypeptides, wherein the first and/or the second polypeptide comprises the two immunomodulatory polypeptides,

wherein the two immunomodulatory polypeptides each comprise a variant interleukin-2 (IL-2) polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:15, and having one or more amino acid substitutions relative to the amino acid sequence set forth in SEQ ID NO:15,

wherein the variant IL-2 polypeptides bind to IL-2 receptor (IL-2R) and exhibit reduced binding affinity to human wild-type IL-2R compared to the binding affinity of a control IL-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:15 for the IL-2R polypeptide when assayed under the same conditions in a bio-layer interferometry (BLI) assay, and

optionally wherein the TMMP comprises an immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold

[0003B] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each of the appended claims.

[0003C] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

BRIEF DESCRIPTION OF THE DRAWINGS

[0004] **FIG. 1** depicts preferential activation of an epitope-specific T cell to a epitope non-specific T-cell by a T-cell modulatory multimeric polypeptide of the present disclosure.

[0005] **FIG. 2A-2G** provide amino acid sequences of immunoglobulin Fc polypeptides.

- [0006] **FIG. 3A-3C** provide amino acid sequences of human leukocyte antigen (HLA) Class I heavy chain polypeptides. Signal sequences are underlined.
- [0007] **FIG. 4** provides a multiple amino acid sequence alignment of beta-2 microglobulin (β 2M) precursors (i.e., including the leader sequence) from *Homo sapiens* (NP_004039.1; SEQ ID NO:49), *Pan troglodytes* (NP_001009066.1; SEQ ID NO:49), *Macaca mulatta* (NP_001040602.1; SEQ ID NO:50), *Bos Taurus* (NP_776318.1; SEQ ID NO:51) and *Mus musculus* (NP_033865.2; SEQ ID NO:52). Amino acids 1-20 are a signal peptide.
- [0008] **FIG. 5A-5K** provide amino acid sequences of examples of suitable HLA heavy chains.
- [0009] **FIG. 6A-6D** are schematic depictions of various T-cell modulatory multimeric polypeptide of the present disclosure.
- [0010] **FIG. 7A-7D** are schematic depictions of various disulfide-linked T-cell modulatory multimeric polypeptide of the present disclosure.
- [0011] **FIG. 8** provides an alignment of eleven mature MHC class I heavy chain peptide sequences without their leader sequences or transmembrane domains.

DEFINITIONS

- [0012] 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.
- [0013] 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.
- [0014] 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.nih.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. Biol. 215:403-10.

- [0015]** 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.
- [0016]** 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.
- [0017]** "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.
- [0018]** 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.

- [0019]** As noted above, an “immunomodulatory polypeptide” (also referred to herein as a “MOD”) specifically binds a cognate co-immunomodulatory polypeptide on a T cell.
- [0020]** An “immunomodulatory domain” (“MOD”) of a T-cell modulatory multimeric polypeptide of the present disclosure binds a cognate co-immunomodulatory polypeptide, which may be present on a target T cell.
- [0021]** “Heterologous,” as used herein, means a nucleotide or polypeptide that is not found in the native nucleic acid or protein, respectively.
- [0022]** “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.
- [0023]** The terms “recombinant expression vector,” or “DNA construct” are used interchangeably herein to refer to a DNA molecule comprising a vector and 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.
- [0024]** 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.

[0025] The term “binding,” as used herein (e.g. with reference to binding of a T-cell modulatory multimeric polypeptide 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., 5×10^{-7} M, 10^{-8} M, 5×10^{-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 μ M to 100 μ M, or from 100 μ M 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.

[0026] 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; 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.

- [0027]** 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.
- [0028]** 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.
- [0029]** 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.
- [0030]** 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.
- [0031]** 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 "multimeric T-cell modulatory 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.

[0032] 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.

[0033] 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

[0034] The present disclosure provides T-cell modulatory multimeric polypeptides that comprise an immunomodulatory polypeptide that exhibits reduced binding affinity to a cognate co-immunomodulatory polypeptide. 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.

T-CELL MODULATORY MULTIMERIC POLYPEPTIDES

[0035] The present disclosure provides a T-cell modulatory multimeric polypeptide (TMMP) comprising: a) a first polypeptide; and b) a second polypeptide, wherein the multimeric polypeptide 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 multimeric polypeptide 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; 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 Fc 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.”

[0036] 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 μ M (e.g., at least 10 μ M, at least 1 μ M, 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 μ M, 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 μ M (e.g., at least 10 μ M, at least 1 μ M, at least 100 nM, at least 10 nM, or at least 1 nM).

[0037] The present disclosure provides a TMMP, wherein the multimeric polypeptide is:

[0038] 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; 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

[0039] 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,

[0040] 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,

[0041] 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

- [0042]** wherein the first polypeptide or the second polypeptide optionally comprises an Ig Fc polypeptide or a non-Ig scaffold; or
- [0043]** 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 multimeric polypeptide 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
- [0044]** 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.

[0045] 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).

[0046] 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 5×10^{-4} M, from about 5×10^{-4} M to about 10^{-5} M, from about 10^{-5} M to 5×10^{-5} M, from about 5×10^{-5} M to 10^{-6} M, from about 10^{-6} M to about 5×10^{-6} M, from about 5×10^{-6} M to about 10^{-7} M, from about 10^{-7} M to about 5×10^{-7} M, from about 5×10^{-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 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, from about 75 μ M to about 100 μ M.

[0047] An immunomodulatory polypeptide present in a TMMP of the present disclosure binds to its cognate co-immunomodulatory polypeptide with an affinity that is 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.

[0048] 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 μ M. 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 μ M, from about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M. 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.

[0049] 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.

[0050] In some cases, a T-cell modulatory polypeptide 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 T-cell modulatory polypeptide 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.

[0051] 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.

- [0052]** 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.
- [0053]** 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 .

- [0054]** 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.
- [0055]** 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.
- [0056]** 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :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, from 10^3 :1 to 10^4 :1, from 10^4 :1 to 10^5 :1, or from 10^5 :1 to 10^6 :1.

- [0057]** 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :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, from 10^3 :1 to 10^4 :1, from 10^4 :1 to 10^5 :1, or from 10^5 :1 to 10^6 :1.
- [0058]** 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :1, at least 10^4 :1, at least 10^5 :1, or at least 10^6 :1.
- [0059]** 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :1, at least 10^4 :1, at least 10^5 :1, or at least 10^6 :1.

[0060] 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :1, at least 10^4 :1, at least 10^5 :1, or at least 10^6 :1.

[0061] 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :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 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :1, at least 10^4 :1, at least 10^5 :1, or at least 10^6 :1.

[0063] 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 μ M 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 5×10^2 :1, at least 10^3 :1, at least 5×10^3 :1, at least 10^4 :1, at least 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.

[0064] 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 multimeric T-cell modulatory polypeptides

[0065] A multimeric T-cell modulatory polypeptide of the present disclosure can be dimerized; i.e., the present disclosure provides a multimeric polypeptide comprising a dimer of a multimeric T-cell modulatory polypeptide of the present disclosure. Thus, the present

disclosure provides a multimeric T-cell modulatory polypeptide 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 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 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 multimeric T-cell modulatory polypeptides 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 β 2-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 both selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1 (CD339), TGF β , CD70, and ICAM. Examples, of suitable MHC polypeptides, immunomodulatory polypeptides, and peptide epitopes are described below.

MHC polypeptides

- [0066]** As noted above, a multimeric polypeptide 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) and MHC Class II polypeptides (e.g., MHC Class II α polypeptide and MHC Class II β polypeptide).
- [0067]** As noted above, in some embodiments of a multimeric polypeptide, the first and the second MHC polypeptides are Class I MHC polypeptides; e.g., in some cases, the first MHC polypeptide is an MHC Class I β 2-microglobulin (β 2M) polypeptide, and the second MHC polypeptide is an MHC Class I heavy chain (H chain). In other cases, the first and the second MHC polypeptides are Class II MHC polypeptides; e.g., in some cases, the first MHC polypeptide is an MHC Class II α -chain polypeptide, and the second MHC polypeptide is an MHC Class II β -chain polypeptide. In other cases, the first polypeptide is an MHC Class II β -chain polypeptide, and the second MHC polypeptide is an MHC Class II α -chain polypeptide.
- [0068]** In some cases, an MHC polypeptide of a multimeric polypeptide 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 multimeric polypeptide is a Class I HLA polypeptide, e.g., a β 2-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. In some cases, an MHC polypeptide of a multimeric polypeptide is a Class II HLA polypeptide, e.g., a Class II HLA α chain or a Class II HLA β chain. MHC Class II polypeptides include MHC Class II DP α and β

polypeptides, DM α and β polypeptides, DOA α and β polypeptides, DOB α and β polypeptides, DQ α and β polypeptides, and DR α and β polypeptides.

[0069] FIG. 8 provides an alignment of eleven mature MHC class I heavy chain peptide sequences without their leader sequences or transmembrane 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 inserted for the formation of a disulfide bond to stabilize the MHC - β 2M complex in the absence of a bound epitope peptide. Also shown in the alignment is position 236 (of the mature polypeptide), which may be substituted by a cysteine residue that can form an intra-chain disulfide bond with β 2M (*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.

[0070] In some cases: i) aa1 (amino acid cluster 1) may be the amino acid sequence GTLRG (SEQ ID NO:219) 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) aa2 (amino acid cluster 2) may be the amino acid sequence YNQSE (SEQ ID NO:220) 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) aa3 (amino acid cluster 3) may be the amino acid sequence TAADM (SEQ ID NO:221) 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) aa4 (amino acid cluster 4) may be the amino acid sequence AQTTK (SEQ ID NO:222) 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) aa5 (amino acid cluster 5) may be the amino acid sequence VETRP (SEQ ID NO:223) 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) aa6 (amino acid cluster 6) may be the amino acid sequence GDGTF (SEQ ID NO:224) 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).

[0071] Table 1 provides examples of HLA Heavy Chains that can be incorporation into a TMMP of the present disclosure.

Table 1

Entry	Base sequence (from Fig. 8)	SEQ ID NO.	Sequence Identity Range	Specific Substitutions at aa positions 84, 139 and/or 236	Substitutions at positions 115 and/or 167
1	HLA-A	242	100%	None	None
2	HLA-A	242	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
3	HLA-B	243	100%	None	None
4	HLA-B	243	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
5	HLA-C	244	100%	None	None
6	HLA-C	244	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
7	HLA-A (var. 1)	53	100%	None	None
8	HLA-A (var. 1)	53	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C

Entry	Base sequence (from Fig. 8)	SEQ ID NO.	Sequence Identity Range	Specific Substitutions at aa positions 84, 139 and/or 236	Substitutions at positions 115 and/or 167
9	MOUSE H2K	54	100%	None	None
10	MOUSE H2K	54	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
11	HLA-A*1101	248	100%	None	None
12	HLA-A*1101	248	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
13	HLA-A*2402	249	100%	None	None
14	HLA-A*2402	249	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C
15	HLA-A*3303	250	100%	None	None
16	HLA-A*3303	250	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; A139C; A236C; (Y84A & A236C); (Y84C & A139C); (Y84C, A139C & A236C)	None; W115C; W167A; or W167C

HLA-A

[0072] As an example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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:

GSLSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE

GPEYWDGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSDW
RFLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRA
YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFYPA
EITLTWQRDGEDQTQDTELVETRPAGDGTGFQKWAAVVVPSGQEQRYTCHVQHE
GLPKPLTLRWE (SEQ ID NO:53).

HLA-A (Y84A; A236C)

[0073] 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:

GSHSMRYFFTSVSRPGRGEPRFIAVGYYDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVKAHSQTHRVDLGTLRGA^YYNQSEAGSHTVQRMYGCDVGSDW
RFLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRA
YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFYPA
EITLTWQRDGEDQTQDTELVETRP^CGDGTGFQKWAAVVVPSGQEQRYTCHVQHE
GLPKPLTLRWE (SEQ ID NO:225), 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 β 2M polypeptide that comprises an R12C substitution.

HLA-A (Y84C; A139C)

[0074] 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:

GSHSMRYFFTSVSRPGRGEPRFIAVGYYDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVKAHSQTHRVDLGTLRG^CYNQSEAGSHTVQRMYGCDVGSDW
RFLRGYHQYAYDGKDYIALKEDLRSWTAADM^CAQTTKHKWEAAHVAEQLRA
YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFYPA
EITLTWQRDGEDQTQDTELVETRPAGDGTGFQKWAAVVVPSGQEQRYTCHVQHE
GLPKPLTLRWE (SEQ ID NO:226), 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-A A11 (HLA-A*1101)

[0075] As one non-limiting example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 A11 heavy chain amino acid sequence: GSHSMRYFYTSVSRPGRGEPRFIAVGYYVDDTQFVRFSDAASQRMEPRAPWIEQ EGPEYWDQETRNVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQIMYGCDVGPDG RFLRGYRQDAYDGKDYIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAY LEGTCVEWLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYP AEI TLTWQRDGEDQTQDTEL VETRPAGDGT FQKWA AVVVPSGEEQRYTCHVQHEGL PKPLTLRWE (SEQ ID NO:227). Such an MHC Class I heavy chain may be prominent in Asian populations, including populations of individuals of Asian descent.

HLA-A A11 (Y84A; A236C)

[0076] As one non-limiting example, in some cases, the MHC Class I heavy chain polypeptide is an HLA-A 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:

GSHSMRYFYTSVSRPGRGEPRFIAVGYYVDDTQFVRFSDAASQRMEPRAPWIEQ EGPEYWDQETRNVKAQSQTDRVDLGTLRGA^YYNQSEDGSHTIQIMYGCDVGPDG RFLRGYRQDAYDGKDYIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAY LEGTCVEWLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYP AEI TLTWQRDGEDQTQDTEL VETRPC^GGDGT FQKWA AVVVPSGEEQRYTCHVQHEGL PKPLTLRWE (SEQ ID NO:228), 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 β 2M polypeptide that comprises an R12C substitution.

HLA-A24 (HLA-A*2402)

[0077] As one non-limiting example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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: GSHSMRYFSTSVSRPGRGEPRFIAVGYYVDDTQFVRFSDAASQRMEPRAPWIEQE GPEYWDEETGKVKAHSQTDRENLRALRYYNQSEAGSHTLQMMFGCDVGS DGR FLRGYHQYAYDGKDYIALKEDLRSWTAADMAAQITKRKWEAAHVAEQQRAYL EGTCVDGLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYP AEITL TWQRDGEDQTQDTEL VETRPAGDGT FQKWA AVVVPSGEEQRYTCHVQHEGLP KPLTLRWE PSSQPTVPIVGIIAGLVLLGAVITGAVVA AVMWRRNSSDRKGGSYSQ

AASSDSAQGSVDVSLTACKV (SEQ ID NO:240). 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)

[0078] As one non-limiting example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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: GSHSMRYFTTSVSRPGRGEPRFIAVGYYDDTQFVRFSDAASQRMEPRAPWIEQE GPEYWDRNTRNVKAHSQIDRVLDGLTRGYYNQSEAGSHTIQMMYGCDVGS DG RFLRGYQQDAYDGKDYIALNEDLRSWTAADMAAQITQRKWEAARVAEQLRAY LEGTCVEWLRRYLENGKETLQRTDPPKTHMTHHAVSDHEATLRCWALSFPYAEI TLTWQRDGEDQTQDTELVETRPAGDGTFFQKWASVVVPSGQEQRYSCHVQHEGL PKPLTLRWEPSQPTIPIVGHAGLVLFAGAVFAAVRWRRKSSDRKGGSYS QAASSDSAQGS DMSLTACKV (SEQ ID NO:241). 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

[0079] As another example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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: GSHSMRYFYTSVSRPGRGEPRFISVGYYDDTQFVRFSDAASPREEPAPWIEQE GPEYWDRNTQIYKAQAQTDRESLRNLRGYYNQSEAGSHTLQSMYGC DVGPDGR LLRGHDQYAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLE GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYPAEITL TWQRDGEDQTQDTELVETRPAGDRTFQKWA AVVVPSGEEQRYSCHVQHEGLPK PLTLRWEPR (SEQ ID NO:229).

HLA-B (Y84A; A236C)

[0080] 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:

GSHSMRYFYTSVSRPGRGEPRFISVGYYVDDTQFVRFDSDAASPREEPRAPWIEQE
GPEYWDRNTQIYKAQAQTDRESLRNLRGA^YYNQSEAGSHTLQSMYGC DVGPDGR
LLRGHDQYAYDGKD^YIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLE
GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYP AEITL
TWQRDGEDQTQDTELVETRP^CGDRTFQKWAAVVVPSGEEQRYTCHVQHEGLPK
PLTLRWE^P (SEQ ID NO:230), 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 β 2M polypeptide that comprises an R12C substitution.

HLA-B (Y84C; A139C)

[0081] 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:

GSHSMRYFYTSVSRPGRGEPRFISVGYYVDDTQFVRFDSDAASPREEPRAPWIEQE
GPEYWDRNTQIYKAQAQTDRESLRNLRG^CYNQSEAGSHTLQSMYGC DVGPDGR
LLRGHDQYAYDGKD^YIALNEDLRSWTAADT^CAQITQRKWEAAREAEQRRAYLE
GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYP AEITL
TWQRDGEDQTQDTELVETRPAGDRTFQKWAAVVVPSGEEQRYTCHVQHEGLPK
PLTLRWE^P (SEQ ID NO:231), 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

[0082] As another example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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:

CSHSMRYFDTA VSRPGRGEPRFISVGYYVDDTQFVRFDSDAASPRGEPRAPWVEQ
EGPEYWDRETQNYKRQAQADR VSLRNLRGYYNQSEDGSHTLQRM YGCDLGPD
GRLLRGYDQSAYDGKD^YIALNEDLRSWTAADTAAQITQRKLEAARAAEQRLRAY
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYP AEI

TLTWQRDGEDQTQDTELVETRPAGDGTQKWA^{AAVVVPSGQE}QRYTCHMQHEG
LQEPLTLSWEP (SEQ ID NO:232).

HLA-C (Y84A; A236C)

[0083] 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:

CSHSMRYFDTA^{VSRPGRGEPRFISVG}YVDDTQFVRFDS^{DAASPRGEPRAPWVEQ}
EGPEYWDRETQNYKRQAQADRVSLRNLRG^AYNQSEDGSHTLQRM^{YGC}DLGPD
GRLLRGYDQSAYDGKD^{YIALNEDLR}SWTAADTAAQITQRKLEAARAAEQ^{LRAY}
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEI
TLTWQRDGEDQTQDTELVETRP^CGDGTQKWA^{AAVVVPSGQE}QRYTCHMQHEG
LQEPLTLSWEP (SEQ ID NO:233), 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 β 2M polypeptide that comprises an R12C substitution.

HLA-C (Y84C; A139C)

[0084] 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:

CSHSMRYFDTA^{VSRPGRGEPRFISVG}YVDDTQFVRFDS^{DAASPRGEPRAPWVEQ}
EGPEYWDRETQNYKRQAQADRVSLRNLRG^CYNQSEDGSHTLQRM^{YGC}DLGPD
GRLLRGYDQSAYDGKD^{YIALNEDLR}SWTAADT^CAQITQRKLEAARAAEQ^{LRAY}
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEI
TLTWQRDGEDQTQDTELVETRPAGDGTQKWA^{AAVVVPSGQE}QRYTCHMQHEG
LQEPLTLSWEP (SEQ ID NO:234), 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.

[0085] A MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 one of the amino acid sequences depicted in FIG. 5A-5K.

- [0086]** As an example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 25-365 of the amino acid sequence of the human HLA-A heavy chain polypeptide depicted in FIG. 3A.
- [0087]** As another example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 25-362 of the amino acid sequence of the human HLA-B heavy chain polypeptide depicted in FIG. 3B.
- [0088]** As another example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 25-362 of the amino acid sequence of the human HLA-C heavy chain polypeptide depicted in FIG. 3C.
- [0089]** As another example, an MHC Class I heavy chain polypeptide of a multimeric polypeptide 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 amino acid sequence:
- [0090]** GPHSLRYFVTAVSRPGLGEPRFIAVG YVDDTQFVRFDSADNPRFEPRAPWMEQ
EGPEYWEEQTQRAKSDEQWFRVSLRTAQRYYNQSKGGSHTFQRMFGCDVGSD
WRLLRGYQQFAYDGRDYIALNEDLKTWTAADTAALITRRKWEQAGDAEYYRA
YLEGECVEWLRRYLELGNETLLRTDSPKAHVITYHPRSQVDVTLRCWALGFYPA
DITLTWQLNGEDLTQDMELVETRPAGDGTQKWA AVVVPLGKEQNYTCHVHH
KGLPEPLTLRW (SEQ ID NO:54).
- [0091]** A β 2-microglobulin (β 2M) polypeptide of a multimeric polypeptide can be a human β 2M polypeptide, a non-human primate β 2M polypeptide, a murine β 2M polypeptide, and the like. In some instances, a β 2M 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 β 2M amino acid sequence depicted in FIG. 4. In some instances, a β 2M 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 β 2M amino acid sequence depicted in FIG. 4.

[0092] In some cases, the MHC Class I heavy chain polypeptide comprises the following amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETR KVKAHSQTHRVDL(aa1){C}(aa2)AGSHTVQRM YGCDVGSDWRF
LRGYHQYAYDGKD YIALKEDLRSW(aa3){C}(aa4)HKWEAAHV AEQLRAYLEGTC
VEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALS FYP AEITLTW
QRDGEDQTQDTEL VETRPAGDGT FQKWA AVVPSGQEQR YTCHVQHEGLPKPL
TLRWE P (SEQ ID NO:238), where the cysteine residues indicated as {C} form an
disulfide bond between the $\alpha 1$ and $\alpha 2-1$ helices. In the sequence above, “aa1” is “amino
acid cluster 1”; “aa2” is “amino acid cluster 2”; “aa3” is “amino acid cluster 3”; and
“aa4” is “amino acid cluster 4”; see, e.g., FIG. 8. An “amino acid cluster” is a cluster of 5
contiguous amino acids, as depicted in FIG. 8.

[0093] In some cases, a suitable $\beta 2M$ polypeptide comprises the following amino acid sequence:

[0094] IQRTPKIQVY SCHPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE
HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTL SQP KIVKWDRDM (SEQ
ID NO:56); and the HLA Class I heavy chain polypeptide comprises the following amino
acid sequence:

[0095] GSHSMRYFFTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETR KVKAHSQTHRVDL(aa1){C}(aa2)AGSHTVQRM YGCDVGSDWRF
LRGYHQYAYDGKD YIALKEDLRSW(aa3){C}(aa4)HKWEAAHV AEQLRAYLEGTC
CWEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALS FYP AEITLT
WQRDGEDQTQDTEL(aa5)(C)(aa6)QKWA AVVPSGQEQR YTCHVQHEGLPKPLT
LRWE P (SEQ ID NO:239), where the cysteine residues indicated as {C} form an
disulfide bond between the $\alpha 1$ and $\alpha 2-1$ helices and the (C) residue forms a disulfide bond
with the $\beta 2M$ 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.

[0096] 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 multimeric polypeptide of the present disclosure, can form a disulfide bond with a cysteine residue present in a second polypeptide chain of a multimeric polypeptide of the present disclosure.

[0097] In some cases, a first MHC polypeptide in a first polypeptide of a multimeric polypeptide, and/or the second MHC polypeptide in the second polypeptide of a multimeric polypeptide, 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.

[0098] For example, in some cases, one of following pairs of residues in an HLA β 2-microglobulin and an HLA Class I heavy chain is substituted with cysteines (where residue numbers are those of the mature polypeptide): 1) β 2M residue 12, HLA Class I heavy chain residue 236; 2) β 2M residue 12, HLA Class I heavy chain residue 237; 3) β 2M residue 8, HLA Class I heavy chain residue 234; 4) β 2M residue 10, HLA Class I heavy chain residue 235; 5) β 2M residue 24, HLA Class I heavy chain residue 236; 6) β 2M residue 28, HLA Class I heavy chain residue 232; 7) β 2M residue 98, HLA Class I heavy chain residue 192; 8) β 2M residue 99, HLA Class I heavy chain residue 234; 9) β 2M residue 3, HLA Class I heavy chain residue 120; 10) β 2M residue 31, HLA Class I heavy chain residue 96; 11) β 2M residue 53, HLA Class I heavy chain residue 35; 12) β 2M residue 60, HLA Class I heavy chain residue 96; 13) β 2M residue 60, HLA Class I heavy chain residue 122; 14) β 2M residue 63, HLA Class I heavy chain residue 27; 15) β 2M residue Arg3, HLA Class I heavy chain residue Gly120; 16) β 2M residue His31, HLA Class I heavy chain residue Gln96; 17) β 2M residue Asp53, HLA Class I heavy chain residue Arg35; 18) β 2M residue Trp60, HLA Class I heavy chain residue Gln96; 19) β 2M residue Trp60, HLA Class I heavy chain residue Asp122; 20) β 2M residue Tyr63, HLA Class I heavy chain residue Tyr27; 21) β 2M residue Lys6, HLA Class I heavy chain residue Glu232; 22) β 2M residue Gln8, HLA Class I heavy chain residue Arg234; 23) β 2M residue Tyr10, HLA Class I heavy chain residue Pro235; 24) β 2M residue Ser11, HLA Class I heavy chain residue Gln242; 25) β 2M residue Asn24, HLA Class I heavy chain residue Ala236; 26) β 2M residue Ser28, HLA Class I heavy chain residue Glu232; 27) β 2M residue Asp98, HLA Class I heavy chain residue His192; and 28) β 2M 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 the amino acid sequence depicted in FIG. 3A, which includes a signal peptide, Gly120 is Gly144; Gln96 is Gln120; etc. In some cases, the β 2M polypeptide comprises an R12C substitution, and the HLA Class I heavy chain comprises an A236C substitution; in such cases, a disulfide bond forms between Cys-12 of the β 2M polypeptide and Cys-236 of the HLA Class I heavy chain. For example, in some cases, residue 236 of the mature HLA-A amino acid sequence (i.e., residue 260 of the amino acid sequence depicted in FIG. 3A) is substituted with a Cys. In some cases, residue 236 of the mature HLA-B amino acid sequence (i.e., residue 260 of the amino acid sequence depicted in FIG. 3B) is substituted with a Cys. In some cases, residue 236 of the mature HLA-C amino acid sequence (i.e., residue 260 of the amino acid sequence depicted in FIG. 3C) is substituted with a Cys. In some cases, residue 32 (corresponding to Arg-12 of mature β 2M) of an amino acid sequence depicted in FIG. 4 is substituted with a Cys.

[0099] In some cases, a β 2M polypeptide comprises the amino acid sequence: IQRTPKIQVY SRHPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTL SQP KIVKWDRDM (SEQ ID NO:55). In some cases, a β 2M polypeptide comprises the amino acid sequence: IQRTPKIQVY SCHPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTL SQP KIVKWDRDM (SEQ ID NO:56).

[00100] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:
 GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
 GPEYWDGETRKYKAHSQTHRVDLGLTRGYYNQSEAGSHTVQRMYGCDVGSWD
 RFLRGYHQYAYDGKDYLKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRA
 YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFPYA
 EITLTWQRDGEDQTQDTEL VETRPAGDGTFQKWAAVVVPSGQEQRYSYCHVQHE
 GLPKPLTLRWEP (SEQ ID NO:53).

[00101] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:
 GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
 GPEYWDGETRKYKAHSQTHRVDLGLTRGYYNQSEAGSHTVQRMYGCDVGSWD
 RFLRGYHQYAYDGKDYLKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRA
 YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFPYA

EITLTWQRDGEDQTQDTELVETRPCGDGTFQKWA AVVVPSGQEQRYTCHVQHE
GLPKPLTLRWE (SEQ ID NO:57).

[00102] In some cases, an HLA Class I heavy chain polypeptide comprises the amino acid sequence:

GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVKAHSQTHRVDLGTLRGAYNQSEAGSHTVQRMYGCDVGS
DW RFLRGYHQYAYDGKDYLKEDLRSWTAADMAAQTTKHKWEAAHVAEQLRA
YLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFP
A EITLTWQRDGEDQTQDTELVETRPCGDGTFQKWA AVVVPSGQEQRYTCHVQHE
GLPKPLTLRWE (SEQ ID NO:58).

[00103] In some cases, the β 2M polypeptide comprises the following amino acid sequence:

[00104] IQRTPKIQVY SCHPAENGKS NFLNCYVSGF HPSDIEVDLLKNGERIEKVE
HSDLSFSKDW SFYLLYYTEF TPTEKDEYAC RVNHVTLSPKIVKWDRDM (SEQ
ID NO:56); and the HLA Class I heavy chain polypeptide of a multimeric polypeptide of
the present disclosure comprises the following amino acid sequence:

[00105] GSHSMRYFFTSVSRPGRGEPRFIAVGYVDDTQFVRFDSDAASQRMEPRAPWIEQ
EGPEYWDGETRKVKAHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGS
DW WRFLRGYHQYAYDGKDYLKEDLRSWTAADMAAQTTKHKWEAAHVAEQLR
AYLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFP
A EITLTWQRDGEDQTQDTELVETRPCGDGTFQKWA AVVVPSGQEQRYTCHVQH
EGLPKPLTLRWE (SEQ ID NO:57), where the Cys residues that are underlined and in
bold form a disulfide bond with one another in the multimeric polypeptide.

[00106] In some cases, the β 2M polypeptide comprises the amino acid sequence:

IQRTPKIQVYSCHPAENGKSNFLNCYVSGFHPSDIEVDLLKNGERIEKVEHSDLSF
SKDWSFYLLYYTEFTPTEKDEYACRVNHVTLSPKIVKWDRDM (SEQ ID
NO:56).

[00107] 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 β 2M 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 introduced as a Y84C substitution. In some cases, the linker connecting the
peptide epitope and the β 2M polypeptide in the first polypeptide chain is GCGGS(G4S)_n
(SEQ ID NO:235), 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 GCGGSGGGSGGGSGGGGS (SEQ ID NO:236). As another example, the linker comprises the amino acid sequence GCGGSGGGSGGGGS (SEQ ID NO:237). Examples of disulfide-linked first and second polypeptides of a multimeric polypeptide of the present disclosure are depicted schematically in FIG. 7A-7D.

Scaffold polypeptides

[00108] A TMMP can comprise an Fc polypeptide, or can comprise another suitable scaffold polypeptide.

[00109] 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., Hassounah 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.

[00110] 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 multimeric polypeptide, compared to a control multimeric polypeptide 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 multimeric polypeptide, compared to a control multimeric polypeptide 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 multimeric polypeptide, compared to a control multimeric polypeptide 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

[00111] In some cases, the first and/or the second polypeptide chain of a multimeric polypeptide comprises an Fc polypeptide. The Fc polypeptide of a multimeric polypeptide 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. 2A-2G. 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. 2A. 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. 2A; 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. 2A; 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. 2A. 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. 2A; 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. 2A. 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. 2B; 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. 2B. 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. 2C; 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. 2C.

[00112] In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc). In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for a substitution of N297 with an amino acid other than asparagine. In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2C (human IgG1 Fc comprising an N297A substitution). In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for a substitution of L234 with an amino acid other than leucine. In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for a substitution of L235 with an amino acid other than leucine.

[00113] In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2E. In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2F. In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2G (human IgG1 Fc comprising an L234A substitution and an L235A substitution). In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for a substitution of P331 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 multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for substitutions at L234 and L235 with amino acids other than leucine.

In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2A (human IgG1 Fc), except for substitutions at L234 and L235 with amino acids other than leucine, and a substitution of P331 with an amino acid other than proline. In some cases, the Fc polypeptide present in a multimeric polypeptide comprises the amino acid sequence depicted in FIG. 2B (human IgG1 Fc comprising L234F, L235E, and P331S substitutions). In some cases, the Fc polypeptide present in a multimeric polypeptide is an IgG1 Fc polypeptide that comprises L234A and L235A substitutions.

Linkers

- [00114]** 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 or Class II 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 or Class II 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 or Class II polypeptide; v) an MHC Class I or Class II 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.
- [00115]** 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.
- [00116]** Exemplary linkers include glycine polymers (G)_n, glycine-serine polymers (including, for example, (GS)_n, (GSGGS)_n (SEQ ID NO:60) and (GGGS)_n (SEQ ID NO:61), 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:62), GGSGG (SEQ ID NO:63), GSGSG (SEQ ID NO:64), GSGGG (SEQ ID NO:65), GGGSG (SEQ ID NO:66), GSSSG (SEQ ID NO:67), and the like. Exemplary linkers can include, e.g., Gly(Ser₄)_n (SEQ ID NO:251), 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:68), where n is 4. In some cases, a linker comprises the amino acid sequence (GSSSS)_n (SEQ ID NO:68), where n is 5. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 1. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 2. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 3. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 4. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 5. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 6. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 7. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 8. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 9. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:69), where n is 10. In some cases, a linker comprises the amino acid sequence AAAGG (SEQ ID NO:70).

[00117] In some cases, a linker polypeptide, present in a first polypeptide of a multimeric polypeptide 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 multimeric polypeptide of the present disclosure. In some cases, for example, a suitable linker comprises the amino acid sequence GCGASGGGGSGGGGS (SEQ ID NO:71). As another example, a suitable linker can comprise the amino acid sequence GCGGS(G4S)_n (SEQ ID NO:235), 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 GCGSGGGGGSGGGSGGGGS (SEQ ID NO:236). As another example, the linker comprises the amino acid sequence GCGSGGGGGSGGGGS (SEQ ID NO:237).

Epitopes

[00118] An epitope present in a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00119] An epitope present in a multimeric polypeptide 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.

[00120] 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-associated 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). In some cases, the epitope is a human papilloma virus E7 antigen epitope; see, e.g., Ramos et al. (2013) *J. Immunother.* 36:66.

[00121] 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, a human papillomavirus (HPV) E6 polypeptide, an LMP2 polypeptide, an HPV E7 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 alpha-fetoprotein (AFP) 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 (PDGFR β) polypeptide, a MAD-CT-2 polypeptide, a Fos-related antigen-1 (FOSL) polypeptide, or a Wilms tumor-1 (WT-1) polypeptide.

[00122] Amino acid sequences of cancer-associated antigens are known in the art; see, e.g., MUC1 (GenBank CAA56734); LMP2 (GenBank CAA47024); HPV E6 (GenBank AAD33252); HPV E7 (GenBank AHG99480); 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); AFP (GenBank NP_001125); 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); FOSL (GenBank NP_005429); and WT-1 (GenBank NP_000369). 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;

[00123] In some cases, the epitope is HPV16E7/82-90 (LLMGTLGIV; SEQ ID NO:72). In some cases, the epitope is HPV16E7/86-93 (TLGIVCPI; SEQ ID NO:73). In some cases, the epitope is HPV16E7/11-20 (YMLDLQPETT; SEQ ID NO:74). In some cases, the epitope

is HPV16E7/11-19 (YMLDLQPET; SEQ ID NO:75). See, e.g., Rensing et al. ((1995) *J. Immunol.* 154:5934) for additional suitable HPV epitopes.

Immunomodulatory polypeptides

[00124] 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.

[00125] 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.

[00126] 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.

[00127] 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.

[00128] 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.

[00129] 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.

[00130] 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.

[00131] 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.

[00132] 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.

[00133] 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.

[00134] 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.

[00135] 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.

[00136] Exemplary pairs of immunomodulatory polypeptide and cognate co-immunomodulatory polypeptide include, but are not limited to:

[00137] a) 4-1BBL (immunomodulatory polypeptide) and 4-1BB (cognate co-immunomodulatory polypeptide);

[00138] b) PD-L1 (immunomodulatory polypeptide) and PD1 (cognate co-immunomodulatory polypeptide);

[00139] c) IL-2 (immunomodulatory polypeptide) and IL-2 receptor (cognate co-immunomodulatory polypeptide);

[00140] d) CD80 (immunomodulatory polypeptide) and CD86 (cognate co-immunomodulatory polypeptide);

[00141] e) CD86 (immunomodulatory polypeptide) and CD28 (cognate co-immunomodulatory polypeptide);

- [00142] f) OX40L (CD252) (immunomodulatory polypeptide) and OX40 (CD134) (cognate co-immunomodulatory polypeptide);
- [00143] g) Fas ligand (immunomodulatory polypeptide) and Fas (cognate co-immunomodulatory polypeptide);
- [00144] h) ICOS-L (immunomodulatory polypeptide) and ICOS (cognate co-immunomodulatory polypeptide);
- [00145] i) ICAM (immunomodulatory polypeptide) and LFA-1 (cognate co-immunomodulatory polypeptide);
- [00146] j) CD30L (immunomodulatory polypeptide) and CD30 (cognate co-immunomodulatory polypeptide);
- [00147] k) CD40 (immunomodulatory polypeptide) and CD40L (cognate co-immunomodulatory polypeptide);
- [00148] l) CD83 (immunomodulatory polypeptide) and CD83L (cognate co-immunomodulatory polypeptide);
- [00149] m) HVEM (CD270) (immunomodulatory polypeptide) and CD160 (cognate co-immunomodulatory polypeptide);
- [00150] n) JAG1 (CD339) (immunomodulatory polypeptide) and Notch (cognate co-immunomodulatory polypeptide);
- [00151] o) JAG1 (immunomodulatory polypeptide) and CD46 (cognate co-immunomodulatory polypeptide);
- [00152] p) CD80 (immunomodulatory polypeptide) and CTLA4 (cognate co-immunomodulatory polypeptide);
- [00153] q) CD86 (immunomodulatory polypeptide) and CTLA4 (cognate co-immunomodulatory polypeptide); and
- [00154] r) CD70 (immunomodulatory polypeptide) and CD27 (cognate co-immunomodulatory polypeptide).
- [00155] 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 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00156] 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 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

PD-L1 variants

[00157] 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.

[00158] A wild-type human PD-L1 polypeptide can comprise the following amino acid sequence: MRIFAVFIFM TYWLLNAFT VTPKDLVYV EYGSNMTIEC
KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD
QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR
ILVVDPTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL
FNVSTSLRIN TTTNEIFYCT FRRLDPEENH TAEVIPGNI LNVSIKICLT LSPST
(SEQ ID NO:1).

[00159] A wild-type human PD-L1 ectodomain can comprise the following amino acid sequence: FT VTPKDL YVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR ILVVDPTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVSTSLRIN TTTNEIFYCT FRRLDPEENH TAEVIPGNI LNVSIKI (SEQ ID NO:2).

[00160] A wild-type PD-1 polypeptide can comprise the following amino acid sequence: PGWFLDSPDR PWNPPTFSPA LLVVTEGDNA TFTCSFSNTS ESFVLNWYRM SPSNQTDKLA AFPEDRSQPG QDCRFRVTQL PNGRDFHMSV VRARRNDSGT YLCGAISLAP KAIKESLRA ELRVTERRAE VPTAHPSPSP RPAGQFQTLV VGVVGGLLS LVLVWVLAV 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.

[00161] 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.

[00162] In some cases, a variant PD-L1 polypeptide has a binding affinity to PD-1 that 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 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00163] 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.

[00164] 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:

[00165] FT VTPK~~X~~LYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG
EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG
ADYKRITVKV NAPYNKINQR ILVVDPTSE HELTCQAEgy PKAEVIWTSS
DHQVLSGKTT TNSKREEKL FNVSTLRIN TTTNEIFYCT FRRLDPEENH

TAEVIPGNI LNVSIKI (SEQ ID NO:76) , where X is any amino acid other than Asp. In some cases, X is Ala. In some cases, X is Arg.

[00166] 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:

[00167] FT VTPPKDLYVV EYGSNMTIEC KFPVEKQLDL AALXVYWEME DKNIIQFVHG
EEDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG
ADYKRITVKV NAPYNKINQR ILVVDPTSE HELTCQAEGY PKAEVIWTSS
DHQVLSGKTT TTNSKREEKL FNVSTLRIN TTTNEIFYCT FRRLDPEENH
TAEVIPGNI LNVSIKI (SEQ ID NO:77), where X is any amino acid other than Ile. In some cases, X is Asp.

[00168] 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:

[00169] FT VTPPKDLYVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG
EXDLKVQHSS YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG
ADYKRITVKV NAPYNKINQR ILVVDPTSE HELTCQAEGY PKAEVIWTSS
DHQVLSGKTT TTNSKREEKL FNVSTLRIN TTTNEIFYCT FRRLDPEENH
TAEVIPGNI LNVSIKI (SEQ ID NO:78), where X is any amino acid other than Glu. In some cases, X is Arg.

CD80 variants

[00170] 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.

[00171] A wild-type amino acid sequence of the ectodomain of human CD80 can be as follows:

[00172] VIHVTKEVATLSC GHNVSVLELA QTRIWQKEK KMLTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESVVLK YEKDAFKREH
LAEVTLVSKA DFPTSPISDF EIPTSNIIRI ICSTSGGFPE PHLRWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:4).

[00173] A wild-type CD28 amino acid sequence can be as follows: MLRLLLLALNL
FPSIQVTGNK ILVKQSPMLV AYDNAVNLSK KYSYNLFSRE FRASLHKGLD
SAVEVCVVYG NYSQQQLQVYS 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.

[00174] A wild-type CD28 amino acid sequence can be as follows: MLRLLLALNL
FPSIQVTGNK ILVKQSPMLV AYDNAVNLSW KHLCPSPFLP GPSKPFWVLV
VVGGLACYS LLVTVAFIIF WVRSKRSRLL HSDYMNMTPR RGPTRKHYQ
PYAPPRDFAA YRS (SEQ ID NO:6)

[00175] A wild-type CD28 amino acid sequence can be as follows: MLRLLLALNL
FPSIQVTGKH LCPSPLFPGP SKPFWVLVVV GVLACYSLL VTVAFIIFWV
RSKRSRLLHS DYMNMTPRRP GPTRKHYQPY APPRDFAAYR S (SEQ ID NO:7).

[00176] 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).

[00177] In some cases, a variant CD80 polypeptide has a binding affinity to CD28 that is from 100 nM to 100 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00178] 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.

[00179] 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:

[00180] VIHVTK EVKEVATLSC GHXVSVEELA QTRIWQKEK KMVLTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTL SVKA DFPTPSISDF EIPTS NIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:79), where X is any amino acid other than Asn. In some cases, X is Ala;

[00181] VIHVTK EVKEVATLSC GHNVSVEELA QTRIWQKEK KMVLTMMMSGD
MNIWPEYKNR TIFDITXNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTL SVKA DFPTPSISDF EIPTS NIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:80), where X is any amino acid other than Asn. In some cases, X is Ala;

[00182] VIHVTK EVKEVATLSC GHNVSVEELA QTRIWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS XVILALRPSD EGTYESCVVLK YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
 WNTTKQEHFP DN (SEQ ID NO:81), where X is any amino acid other than Ile. In some cases, X is Ala;

[00183] VIHVTK EVKEVATLSC GHNVSVEELA QTRIWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLX YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
 WNTTKQEHFP DN (SEQ ID NO:82), where X is any amino acid other than Lys. In some cases, X is Ala;

[00184] VIHVTK EVKEVATLSC GHNVSVEELA QTRIWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS XDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
 WNTTKQEHFP DN (SEQ ID NO:83), where X is any amino acid other than Gln. In some cases, X is Ala;

[00185] VIHVTK EVKEVATLSC GHNVSVEELA QTRIWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS QXPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
 WNTTKQEHFP DN (SEQ ID NO:84), where X is any amino acid other than Asp. In some cases, X is Ala;

[00186] VIHVTK EVKEVATLSC GHNVSVEEXA QTRIWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
 WNTTKQEHFP DN (SEQ ID NO:85), where X is any amino acid other than Leu. In some cases, X is Ala;

[00187] VIHVTK EVKEVATLSC GHNVSVEELA QTRIXWQKEK KMVLTMMMSGD
 MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
 LAEVTLSVKA DFPTPSISDF EIPTSNIIRRI ICSTSGGFPE PHLSWLENGE
 ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN

WNTTKQEHFP DN (SEQ ID NO:86), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00188] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYXKEK KMLVTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTLNVKA DFPTPSISDF EIPTSNIIRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:87), where X is any amino acid other than Gln. In some cases, X is Ala;

[00189] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYQKEK KXMLVTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTLNVKA DFPTPSISDF EIPTSNIIRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:88), where X is any amino acid other than Met. In some cases, X is Ala;

[00190] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYQKEK KMXMLVTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTLNVKA DFPTPSISDF EIPTSNIIRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:89), where X is any amino acid other than Val. In some cases, X is Ala;

[00191] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYQKEK KMLVTMMMSGD
MNXWPEYKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTLNVKA DFPTPSISDF EIPTSNIIRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:90), where X is any amino acid other than Ile. In some cases, X is Ala;

[00192] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYQKEK KMLVTMMMSGD
MNIWPEXKNR TIFDITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH
LAEVTLNVKA DFPTPSISDF EIPTSNIIRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:91), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00193] VIHVTKEVKEVATLSC GHNVSVVEELA QTRIWYQKEK KMLVTMMMSGD
MNIWPEYKNR TIFXITNNLS IVILALRPSD EGTYESCVVLK YEKDAFKREH

LAEVTL SVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:92), where X is any amino acid other than Asp. In
some cases, X is Ala;

[00194] VIHVTK EVKEVATLSC GHNVSV EELA QTRIWQKEK KMVLTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH
LAEVTL SVKA DXPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:93), where X is any amino acid other than Phe. In
some cases, X is Ala;

[00195] VIHVTK EVKEVATLSC GHNVSV EELA QTRIWQKEK KMVLTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH
LAEVTL SVKA DFPTPSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVX QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:94), where X is any amino acid other than Ser. In
some cases, X is Ala; and

[00196] VIHVTK EVKEVATLSC GHNVSV EELA QTRIWQKEK KMVLTMMMSGD
MNIWPEYKNR TIFDITNNLS IVILALRPSD EGTYECVVLK YEKDAFKREH
LAEVTL SVKA DFPTXSISDF EIPTSNIRRI ICSTSGGFPE PHLSWLENGE
ELNAINTTVS QDPETELYAV SSKLDFNMTT NHSFMCLIKY GHLRVNQTFN
WNTTKQEHFP DN (SEQ ID NO:95), where X is any amino acid other than Pro. In
some cases, X is Ala.

CD86 variants

[00197] 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.

[00198] The amino acid sequence of the full ectodomain of a wild-type human CD86 can be as
follows:

APLKI QAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSLSVLANFSQPEIVP
ISNITENVYINLTCSIIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSISL
SVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPPPPDHIP (SEQ ID NO:8).

[00199] The amino acid sequence of the IgV domain of a wild-type human CD86 can be as follows:

APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKYM
NRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVL (SEQ ID
 NO:9) .

[00200] 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).

[00201] In some cases, a variant CD86 polypeptide has a binding affinity to CD28 that is from 100 nM to 100 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00202] 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.

[00203] 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.

[00204] 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:

[00205] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MXRTSFDSDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVLANFSQPEIV
 PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
 LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:96),
 where X is any amino acid other than Asn. In some cases, X is Ala;

[00206] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFXSDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVLANFSQPEIV
 PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
 LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:97),
 where X is any amino acid other than Asp. In some cases, X is Ala;

[00207] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFDSDSXTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVLANFSQPEIV
 PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
 LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:98),
 where X is any amino acid other than Trp. In some cases, X is Ala;

[00208] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFDSDSWTLRLHNLQIKDKGLYQCI IHXKKPTGMIRIHQMNSELSVLANFSQPEIV
 PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
 LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:99),
 where X is any amino acid other than His. In some cases, X is Ala;

[00209] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MXRTSFDSDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVL (SEQ ID
 NO:100), where X is any amino acid other than Asn. In some cases, X is Ala;

[00210] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFXSDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVL (SEQ ID
 NO:101), where X is any amino acid other than Asp. In some cases, X is Ala;

[00211] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFDSDSXTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVL (SEQ ID
 NO:102), where X is any amino acid other than Trp. In some cases, X is Ala;

[00212] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLVLNEVYLGKEKFDSVHISKY
 MNRTSFDSDSWTLRLHNLQIKDKGLYQCI IHXKKPTGMIRIHQMNSELSVL (SEQ ID
 NO:103), where X is any amino acid other than His. In some cases, X is Ala;

[00213] APLKIQAYFNETADLPCQFANSQNQSLSELVFWQDQENLXLNEVYLGKEKFDSVHISKY
 MNRTSFDSDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVLANFSQPEIV

PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
LSVSFPDVTSNMTIFCILETDKTRLSSPFSIELEDPQPPPDHIP (SEQ ID NO:104),

where X is any amino acid other than Val. In some cases, X is Ala;

[00214] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLXLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVL (SEQ ID
NO:105), where X is any amino acid other than Val. In some cases, X is Ala;

[00215] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVLANFSQPEIV
PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
LSVSFPDVTSNMTIFCILETDKTRLSSPFSIELEDPQPPPDHIP (SEQ ID NO:106),
where X is any amino acid other than Gln. In some cases, X is Ala;

[00216] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVL (SEQ ID
NO:107), where X is any amino acid other than Gln. In some cases, X is Ala;

[00217] APLKIQAYFNETADLPCQFANSQNQSLSELVVXWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVLANFSQPEIV
PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
LSVSFPDVTSNMTIFCILETDKTRLSSPFSIELEDPQPPPDHIP (SEQ ID NO:108),
where X is any amino acid other than Phe. In some cases, X is Ala;

[00218] APLKIQAYFNETADLPCQFANSQNQSLSELVVXWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVL (SEQ ID
NO:109), where X is any amino acid other than Phe. In some cases, X is Ala;

[00219] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTXRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVLANFSQPEIV
PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
LSVSFPDVTSNMTIFCILETDKTRLSSPFSIELEDPQPPPDHIP (SEQ ID NO:110),
where X is any amino acid other than Leu. In some cases, X is Ala;

[00220] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHISKY
MNRTSFDSDSWTXRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVL (SEQ ID
NO:111), where X is any amino acid other than Leu. In some cases, X is Ala;

[00221] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHISKX
MNRTSFDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVLANFSQPEIV
PISNITENVYINLTCSSIHGYPEPKKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS

LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:112),
where X is any amino acid other than Tyr. In some cases, X is Ala;

[00222] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKX
MNRTSFDSWTLRLHNLQIKDKGLYQCI IHHKKPTGMIRIHQMNSELSVL (SEQ ID
NO:113), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00223] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MXRTSFDSWTLRLHNLQIKDKGLYQCI IHXKKPTGMIRIHQMNSELSVLANFSQPEIV
PISNITENVYINLTCSSIHGYPEPKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVSIS
LSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:114),
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;

[00224] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MXRTSFDSWTLRLHNLQIKDKGLYQCI IHXKKPTGMIRIHQMNSELSVL (SEQ ID
NO:115), 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;

[00225] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MNRTSFX₁SDSWTLRLHNLQIKDKGLYQCI IHX₂KKPTGMIRIHQMNSELSVLANFSQPE
IVPISNITENVYINLTCSSIHGYPEPKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVS
ISLSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:116),
where X₁ is any amino acid other than Asp, and X₂ is any amino acid other than His . In
some cases, X₁ is Ala and X₂ is Ala;

[00226] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MNRTSFX₁SDSWTLRLHNLQIKDKGLYQCI IHX₂KKPTGMIRIHQMNSELSVL (SEQ ID
NO:117), 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;

[00227] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MX₁RTSFX₂SDSWTLRLHNLQIKDKGLYQCI IHX₃KKPTGMIRIHQMNSELSVLANFSQPE
IVPISNITENVYINLTCSSIHGYPEPKMSVLLRTKNSTIEYDGIMQKSQDNVTELYDVS
ISLSVSFPDVTSNMTIFCILETDKTRLLSSPFSIELEDPQPPDHIP (SEQ ID NO:118),
where X₁ is any amino acid other than Asn, X₂ is any amino acid other than Asp, and X₃
is any amino acid other than His . In some cases, X₁ is Ala, X₂ is Ala, and X₃ is Ala; and

[00228] APLKIQAYFNETADLPCQFANSQNQSLSELVVFWDQENLVLNEVYLGKEKFDSVHSKY
MX₁RTSFX₂SDSWTLRLHNLQIKDKGLYQCI IHX₃KKPTGMIRIHQMNSELSVL (SEQ ID
NO:119), where X₁ is any amino acid other than Asn, X₂ is any amino acid other than

Asp, and X₃ is any amino acid other than His . In some cases, X₁ is Ala, X₂ is Ala, and X₃ is Ala.

4-1BBL variants

[00229] 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).

[00230] 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 RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:10).

[00231] In some cases, a variant 4-1BBL polypeptide is a variant of the tumor necrosis factor (TNF) homology domain (THD) of human 4-1BBL.

[00232] 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:

[00233] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:11).

[00234] D PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:12).

[00235] D PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPA (SEQ ID NO:13).

[00236] A wild-type 4-1BB amino acid sequence can be as follows: MGNSCYNIVA TLLLVLNFER TRSLQDPCSN CPAGTFCDNN RNQICSPCPP NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS MCEQDCKQGG ELTKKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG TKERDVVCGP SPADLSPGAS SVTPPAPARE PGHSPQIISF FLALTSTALL FLLFFLT LRF

SVVKRGRKKL LYIFKQPFMR PVQTTQEEDG CSCRFPEEEEE 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.

[00237] 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.

[00238] In some cases, a variant 4-1BBL polypeptide has a binding affinity to 4-1BB that is from 100 nM to 100 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00239] 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.

[00240] 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:

[00241] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYXEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:120), where X is any amino acid other than Lys. In some cases, X is Ala;

[00242] PAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWXLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:121), where X is any amino acid other than Gln. In some cases, X is Ala;

[00243] PAGLLDLRQG XFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:122), where X is any amino acid other than Met. In some cases, X is Ala;

[00244] PAGLLDLRQG MXAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA

LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:123), where X is any amino acid
other than Phe. In some cases, X is Ala;

[00245] PAGLLDLRQG MFAXLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:124), where X is any amino acid
other than Gln. In some cases, X is Ala;

[00246] PAGLLDLRQG MFAQXV AQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:125), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00247] PAGLLDLRQG MFAQLXAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:126), where X is any amino acid
other than Val. In some cases, X is Ala;

[00248] PAGLLDLRQG MFAQLVAXNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:127), where X is any amino acid
other than Gln. In some cases, X is Ala;

[00249] PAGLLDLRQG MFAQLVAQXV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:128), where X is any amino acid
other than Asn. In some cases, X is Ala;

[00250] PAGLLDLRQG MFAQLVAQNX LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:129), where X is any amino acid
other than Val. In some cases, X is Ala;

[00251] PAGLLDLRQG MFAQLVAQNV XLIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:130), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00252] PAGLLDLRQG MFAQLVAQNV LXIDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:131), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00253] PAGLLDLRQG MFAQLVAQNV LLXDGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:132), where X is any amino acid
other than Ile. In some cases, X is Ala;

[00254] PAGLLDLRQG MFAQLVAQNV LLIXGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:133), where X is any amino acid
other than Asp. In some cases, X is Ala;

[00255] PAGLLDLRQG MFAQLVAQNV LLIDXPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:134), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00256] PAGLLDLRQG MFAQLVAQNV LLIGGXLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:135), where X is any amino acid
other than Pro. In some cases, X is Ala;

[00257] PAGLLDLRQG MFAQLVAQNV LLIGGPXSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ

GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:136), where X is any amino acid other than Leu. In some cases, X is Ala;

[00258] PAGLLDLRQG MFAQLVAQNV LLIGGPLXWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:137), where X is any amino acid other than Ser. In some cases, X is Ala;

[00259] PAGLLDLRQG MFAQLVAQNV LLIGGPLSXY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:138), where X is any amino acid other than Trp. In some cases, X is Ala;

[00260] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWX SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:139), where X is any amino acid other than Tyr. In some cases, X is Ala;

[00261] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY XDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:140), where X is any amino acid other than Ser. In some cases, X is Ala;

[00262] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SXPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:141), where X is any amino acid other than Asp. In some cases, X is Ala;

[00263] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDXGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:142), where X is any amino acid other than Pro. In some cases, X is Ala;

[00264] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPXLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA

LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:143), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00265] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGXAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:144), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00266] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAXVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:145), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00267] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGXSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:146), where X is any amino acid
other than Val. In some cases, X is Ala;

[00268] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVXL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:147), where X is any amino acid
other than Ser. In some cases, X is Ala;

[00269] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSX TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:148), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00270] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL XGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:149), where X is any amino acid
other than Thr. In some cases, X is Ala;

[00271] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TXGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:150), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00272] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGXLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:151), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00273] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGXSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:152), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00274] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLXYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:153), where X is any amino acid
other than Ser. In some cases, X is Ala;

[00275] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSXKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:154), where X is any amino acid
other than Tyr. In some cases, X is Ala;

[00276] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKXDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:155), where X is any amino acid
other than Glu. In some cases, X is Ala;

[00277] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEXT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ

GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:156), where X is any amino acid other than Asp. In some cases, X is Ala;

[00278] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDX
 KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ
 GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:157), where X is any amino acid other than Thr. In some cases, X is Ala;

[00279] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
XELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ
 GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:158), where X is any amino acid other than Lys. In some cases, X is Ala;

[00280] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
 KXLVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ
 GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:159), where X is any amino acid other than Glu. In some cases, X is Ala;

[00281] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
 KELVVAKAGV YYVXFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ 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;

[00282] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
 KELVVAKAGV YYVFXQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ
 GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:161), where X is any amino acid other than Phe. In some cases, X is Ala;

[00283] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
 KELVVAKAGV YYVFFXLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
 LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVHLHTEA RARHAWQLTQ
 GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:162), where X is any amino acid other than Gln. In some cases, X is Ala;

[00284] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
 KELVVAKAGV YYVFFQXELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA

LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:163), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00285] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLXLR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:164), where X is any amino acid
other than Glu. In some cases, X is Ala;

[00286] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLEXR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:165), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00287] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELX RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:166), where X is any amino acid
other than Arg. In some cases, X is Ala;

[00288] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR XVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:167), where X is any amino acid
other than Arg. In some cases, X is Ala;

[00289] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RXVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:168), where X is any amino acid
other than Val. In some cases, X is Ala;

[00290] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVXAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:169), where X is any amino acid
other than Val. In some cases, X is Ala;

[00291] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAXEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:170), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00292] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGXGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:171), where X is any amino acid
other than Glu. In some cases, X is Ala;

[00293] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEXSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:172), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00294] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGXGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:173), where X is any amino acid
other than Ser. In some cases, X is Ala;

[00295] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVXLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:174), where X is any amino acid
other than Asp. In some cases, X is Ala;

[00296] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDXPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:175), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00297] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLXPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ

GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:176), where X is any amino acid other than Pro. In some cases, X is Ala;

[00298] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPAXS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:177), where X is any amino acid other than Ser. In some cases, X is Ala;

[00299] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASX EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:178), where X is any amino acid other than Ser. In some cases, X is Ala;

[00300] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS XARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:179), where X is any amino acid other than Glu. In some cases, X is Ala;

[00301] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EAXNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:180), where X is any amino acid other than Arg. In some cases, X is Ala;

[00302] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARXSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:181), where X is any amino acid other than Asn. In some cases, X is Ala;

[00303] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNXAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:182), where X is any amino acid other than Ser. In some cases, X is Ala;

[00304] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA

LTVDLPPASS EARNSAXGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:183), where X is any amino acid
other than Phe. In some cases, X is Ala;

[00305] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGX RLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:184), where X is any amino acid
other than Gln. In some cases, X is Ala;

[00306] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ XLGVLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:185), where X is any amino acid
other than Arg. In some cases, X is Ala;

[00307] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RXGVHLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:186), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00308] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLXVHLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:187), where X is any amino acid
other than Gly. In some cases, X is Ala;

[00309] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGXHLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:188), where X is any amino acid
other than Val. In some cases, X is Ala;

[00310] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVXLHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:189), where X is any amino acid
other than His. In some cases, X is Ala;

[00311] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VH~~XHTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:190), where X is any amino acid
other than Leu. In some cases, X is Ala;

[00312] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHL~~XTEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:191), where X is any amino acid
other than His. In some cases, X is Ala;

[00313] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHLH~~XEA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:192), where X is any amino acid
other than Thr. In some cases, X is Ala;

[00314] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHLHT~~XA RARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:193), where X is any amino acid
other than Glu. In some cases, X is Ala;

[00315] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHLHTEA~~ XARHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:194), where X is any amino acid
other than Arg. In some cases, X is Ala;

[00316] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHLHTEA~~ RAXHAWQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:195), where X is any amino acid
other than Arg. In some cases, X is Ala;

[00317] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLG~~VHLHTEA~~ RARXAWQLTQ

GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:196), where X is any amino acid other than His. In some cases, X is Ala;

[00318] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAXQLTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:197), where X is any amino acid other than Trp. In some cases, X is Ala;

[00319] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQXTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:198), where X is any amino acid other than Leu. In some cases, X is Ala;

[00320] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLXTQ
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:199), where X is any amino acid other than Thr. In some cases, X is Ala;

[00321] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTX
GATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:200), where X is any amino acid other than Gln. In some cases, X is Ala;

[00322] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
XATVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:201), where X is any amino acid other than Gly. In some cases, X is Ala;

[00323] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA
LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GAXVLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:202), where X is any amino acid other than Thr. In some cases, X is Ala; and

[00324] PAGLLDLRQG MFAQLVAQNV LLIGGPLSWY SDPGLAGVSL TGGLSYKEDT
KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA

LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ
GATXLGLFRV TPEIPAGLPS PRSE (SEQ ID NO:203), where X is any amino acid
other than Val. In some cases, X is Ala.

IL-2 variants

[00325] 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-2R α , IL-2R β , and IL-2R γ .

[00326] A wild-type IL-2 amino acid sequence can be as follows: APTSSSTKKT

QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA
TELKHLQCLEEELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNRWITFCQSIIS TLT (SEQ ID NO:15).

[00327] 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-2R α ; also
referred to as CD25), a beta chain (IL-2R β ; also referred to as CD122; and a gamma
chain (IL-2R γ ; also referred to as CD132). Amino acid sequences of human IL-2R α ,
IL2R β , and IL-2R γ can be as follows.

[00328] Human IL-2R α : ELCDDDPPE IPHATFKAMA YKEGTMLNCE CKRGFRRIKS
GSLYMLCTGN SSHSSWDNQC QCTSSATRNT TKQVTPQPEE QKERKTTEMQ
SPMQPVDQAS LPGHCREPPP WENEATERIY HFVVGMVYYY QCVQGYRALH
RGPAESVCKM THGKTRWTQP QLICTGEMET SQFPGEKPKQ ASPEGRPESE
TSCLVTTTDF QIQTEMAATM ETSIFTTEYQ VAVAGCVFLL ISVLLLSGLT
WQRRQRKSRR TI (SEQ ID NO:16).

[00329] Human IL-2R β : VNG TSQFTCFYNS RANISCVWSQ DGALQDTSCQ
VHAWPDRRRW NQTCELLPVS QASWACNLIL GAPDSQKLTT VDIVTLRVLC
REGVRWRVMA IQDFKPFENL RLMAPIQLQV VHVETHRCNI SWEISQASHY
FERHLEFEAR TLSPGHTWEE APLLTLKQKQ EWICLETLTP DTQYEFQVRV
KPLQGEFTTW SPWSQPLAFR TKPAALGKDT IPWLGHLVVG LSGAFGFIL
VYLLINCRNT GPWLKKVLKC NTPDPSKFFS QLSSEHGGDV QKWLSSPFPS
SSFSPGGLAP EISPLEVLER DKVTQLLLQQ DKVPEPASLS SNHSLTSCFT
NQGYFFFHLP DALEIEACQV YFTYDPYSEE DPDEGVAGAP TGSSPQPLQP
LSGEDDAYCT FPSRDDLLLF SPSLLGGPSP PSTAPGGSGA GEERMPPSLQ
ERVPRDWDPO PLGPPTPGVP DLVDFQPPPE LVLREAGEEV PDAGPREGVS
FPWSRPPGQG EFRALNARLP LNTDAYLSLQ ELQGQDPTHL V (SEQ ID NO:17).

[00330] Human IL-2R γ : LNTTILTP NGNEDTTADF FLTTMPTDSL SVSTLPLPEV
 QCFVFNVEYM NCTWNSSSEP QPTNLTLYHW YKNSDNDKVQ KCSHYLFSEE
 ITSGCQLQKK EIHL YQTFVV QLQDPREPRR QATQMLKLQN LVIPWAPENL
 TLHKLSesQL ELNWN NRFLN HCLEHLVQYR TDWDHSWTEQ SVDYRHKFSL
 PSVDGQKRYT FRVRSRFNPL CGSAQHWSEW SHPIHWGSNT SKENPFLFAL
 EAVVISVGSM GLIISLLCVY FWLERTMPRI PTLKNLEDLV TEYHGNFSAW
 SGVSKGLAES LQPDYSERLC LVSEIPP KGG ALGEGPGASP CNQHSPYWAP
 PCYTLKPET (SEQ ID NO:18).

[00331] 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.

[00332] 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.

[00333] In some cases, a variant IL-2 polypeptide has a binding affinity to IL-2R that is from 100 nM to 100 μ M. 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 μ M, to about 1 μ M to about 5 μ M, from about 5 μ M to about 10 μ M, from about 10 μ M to about 15 μ M, from about 15 μ M to about 20 μ M, from about 20 μ M to about 25 μ M, from about 25 μ M to about 50 μ M, from about 50 μ M to about 75 μ M, or from about 75 μ M to about 100 μ M.

[00334] 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.

[00335] 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:

[00336] APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML T~~X~~KFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:19), where X is any amino acid other than Phe. In some cases, X is Ala;

[00337] APTSSSTKKT QLQLEHLLL~~X~~ LQMILNGINN YKNPKLTRML TFKFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:20), where X is any amino acid other than Asp. In some cases, X is Ala;

[00338] APTSSSTKKT QLQL~~X~~HLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:21), where X is any amino acid other than Glu. In some cases, X is Ala;

[00339] APTSSSTKKT QLQLEXLLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:22), where X is any
 amino acid other than His. In some cases, X is Ala;

[00340] APTSSSTKKT QLQLEXLLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:22), 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. In 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;

[00341] APTSSSTKKT QLQLEHLLLLD LQMILNGINN YKNPKLTRML TFKFXMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:23), where X is any
 amino acid other than Tyr. In some cases, X is Ala;

[00342] APTSSSTKKT QLQLEHLLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCXSIIS TLT (SEQ ID NO:24), where X is any
 amino acid other than Gln. In some cases, X is Ala;

[00343] APTSSSTKKT QLQLEX₁LLLLD LQMILNGINN YKNPKLTRML TX₂KFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:25), where X₁ is any
 amino acid other than His, and where X₂ is any amino acid other than Phe. In some cases,
 X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₁ is Ala; and X₂ is Ala;

[00344] APTSSSTKKT QLQLEHLLLLX₁ LQMILNGINN YKNPKLTRML TX₂KFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:26), where X₁ is any
 amino acid other than Asp; and where X₂ is any amino acid other than Phe. In some
 cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₁ is Ala; and X₂ is Ala;

[00345] APTSSSTKKT QLQLEX₁HLLLX₂ LQMILNGINN YKNPKLTRML TX₃KFYMPKKA
 TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
 TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:27), where X₁ is any

amino acid other than Glu; where X₂ is any amino acid other than Asp; and where X₃ is any amino acid other than Phe. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₁ is Ala; X₂ is Ala; and X₃ is Ala;

[00346] APTSSSTKKT QLQLEX₁LLLX₂ LQMILNGINN YKNPKLTRML TX₃KFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:28), where X₁ is any amino acid other than His; where X₂ is any amino acid other than Asp; and where X₃ is any amino acid other than Phe. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₁ is Ala; X₂ is Ala; and X₃ is Ala;

[00347] APTSSSTKKT QLQLEHLLLX₁ LQMILNGINN YKNPKLTRML TX₂KFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCX₃SIIS TLT (SEQ ID NO:29), where X₁ is any amino acid other than Asp; where X₂ is any amino acid other than Phe; and where X₃ is any amino acid other than Gln. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₁ is Ala; X₂ is Ala; and X₃ is Ala;

[00348] APTSSSTKKT QLQLEHLLLX₁ LQMILNGINN YKNPKLTRML TX₂KFX₃MPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:30), where X₁ is any amino acid other than Asp; where X₂ is any amino acid other than Phe; and where X₃ is any amino acid other than Tyr. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₁ is Ala; X₂ is Ala; and X₃ is Ala;

[00349] APTSSSTKKT QLQLEX₁LLLX₂ LQMILNGINN YKNPKLTRML TX₃KFX₄MPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT (SEQ ID NO:31), where X₁ is any amino acid other than His; where X₂ is any amino acid other than Asp; where X₃ is any amino acid other than Phe; and where X₄ is any amino acid other than Tyr. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₄ is Ala. In some cases, X₁ is Ala; X₂ is Ala; X₃ is Ala; and X₄ is Ala;

[00350] APTSSSTKKT QLQLEHLLLX₁ LQMILNGINN YKNPKLTRML TX₂KFX₃MPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCX₄SIIS TLT (SEQ ID NO:32), where X₁ is any amino acid other than Asp; where X₂ is any amino acid other than Phe; where X₃ is any amino acid other than Tyr; and where X₄ is any amino acid other than Gln. In some cases,

X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₄ is Ala. In some cases, X₁ is Ala; X₂ is Ala; X₃ is Ala; and X₄ is Ala;

[00351] APTSSSTKKT QLQLEX₁LLLX₂ LQMILNGINN YKNPKLTRML TX₃KFX₄MPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCX₅SIIS TLT (SEQ ID NO:33), where X₁ is any amino acid other than His; where X₂ is any amino acid other than Asp; where X₃ is any amino acid other than Phe; where X₄ is any amino acid other than Tyr; and where X₅ is any amino acid other than Gln. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₄ is Ala. In some cases, X₅ is Ala. In some cases, X₁ is Ala; X₂ is Ala; X₃ is Ala; X₄ is Ala; X₅ is Ala; and

[00352] APTSSSTKKT QLQLEX₁LLLD LQMILNGINN YKNPKLTRML TX₂KFYMPKKA
TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE
TTFMCEYADE TATIVEFLNR WITFCX₃SIIS TLT (SEQ ID NO:34), where X₁ is any amino acid other than His; where X₂ is any amino acid other than Phe; and where X₃ is any amino acid other than Gln. In some cases, X₁ is Ala. In some cases, X₂ is Ala. In some cases, X₃ is Ala. In some cases, X₁ is Ala; X₂ is Ala; and X₃ is Ala.

Additional polypeptides

[00353] A polypeptide chain of a multimeric polypeptide 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 multimeric polypeptide, at the C-terminus of a polypeptide chain of a multimeric polypeptide, or internally within a polypeptide chain of a multimeric polypeptide.

Epitope tag

[00354] Suitable epitope tags include, but are not limited to, hemagglutinin (HA; e.g., YPYDVPDYA (SEQ ID NO:35); FLAG (e.g., DYKDDDDK (SEQ ID NO:36); c-myc (e.g., EQKLISEEDL; SEQ ID NO:37), and the like.

Affinity domain

[00355] 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:38), HisX6 (HHHHHH) (SEQ ID

NO:39), C-myc (EQKLISEEDL) (SEQ ID NO:37), Flag (DYKDDDDK) (SEQ ID NO:36), StrepTag (WSHPQFEK) (SEQ ID NO:40), hemagglutinin, e.g., HA Tag (YPYDVPDYA) (SEQ ID NO:35), glutathione-S-transferase (GST), thioredoxin, cellulose binding domain, RYIRS (SEQ ID NO:41), Phe-His-His-Thr (SEQ ID NO:42), chitin binding domain, S-peptide, T7 peptide, SH2 domain, C-end RNA tag, WEAAAREACCRECCARA (SEQ ID NO:43), 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

[00356] A polypeptide chain of a multimeric polypeptide of the present disclosure can comprise a small molecule drug linked (e.g., covalently attached) to the polypeptide chain. For example, where a multimeric polypeptide 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 multimeric polypeptide of the present disclosure can comprise a cytotoxic agent linked (e.g., covalently attached) to the polypeptide chain. For example, where a multimeric polypeptide of the present disclosure comprises an Fc polypeptide, the Fc polypeptide can comprise a covalently linked cytotoxic agent. Cytotoxic agents include prodrugs.

[00357] A drug (e.g., a cancer chemotherapeutic agent) can be linked directly or indirectly to a polypeptide chain of a multimeric polypeptide of the present disclosure. For example, where a multimeric polypeptide 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 multimeric polypeptide of the present disclosure via a thioether bond, an amide bond, a carbamate bond, a disulfide bond, or an ether bond.

[00358] 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-iodoacetyl)aminobenzoate (SIAB); 6-maleimidocaproyl (MC); maleimidopropanoyl (MP); p-aminobenzoyloxycarbonyl (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).

[00359] 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.

[00360] For example, where a multimeric polypeptide 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).

[00361] 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.

[00362] 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.

[00363] 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; gelatin; 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.

METHODS OF GENERATING A MULTIMERIC T-CELL MODULATORY POLYPEPTIDE

[00364] 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.

[00365] 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.

[00366] In some cases, a parental wild-type immunomodulatory polypeptide and cognate immunomodulatory polypeptide pairs are selected from:

[00367] IL-2 and IL-2 receptor;

[00368] 4-1BBL and 4-1BB;

[00369] PD-L1 and PD-1;

[00370] CD70 and CD27;

[00371] TGF β and TGF β receptor;

[00372] CD80 and CD28;

[00373] CD86 and CD28;

[00374] OX40L and OX40;

[00375] FasL and Fas;

[00376] ICOS-L and ICOS;

[00377] ICAM and LFA-1;

[00378] JAG1 and Notch;

[00379] JAG1 and CD46;

[00380] CD80 and CTLA4; and

[00381] CD86 and CTLA4.

[00382] 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.

[00383] 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.

[00384] 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 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; TGF β and TGF β 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.

[00385] 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.

[00386] 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.

[00387] 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 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; TGF β and TGF β 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

[00388] 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.

[00389] The present disclosure provides nucleic acids comprising nucleotide sequences encoding a multimeric polypeptide of the present disclosure. In some cases, the individual polypeptide chains of a multimeric polypeptide of the present disclosure are encoded in separate nucleic acids. In some cases, all polypeptide chains of a multimeric polypeptide 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 multimeric polypeptide of the present disclosure; and a second nucleic acid comprises a nucleotide sequence encoding a second polypeptide of a multimeric polypeptide of the present disclosure. In some cases, single nucleic acid comprises a nucleotide sequence encoding a

first polypeptide of a multimeric polypeptide of the present disclosure and a second polypeptide of a multimeric polypeptide of the present disclosure.

Separate nucleic acids encoding individual polypeptide chains of a multimeric polypeptide

[00390] The present disclosure provides nucleic acids comprising nucleotide sequences encoding a multimeric polypeptide of the present disclosure. As noted above, in some cases, the individual polypeptide chains of a multimeric polypeptide of the present disclosure are encoded in separate nucleic acids. In some cases, nucleotide sequences encoding the separate polypeptide chains of a multimeric polypeptide 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.

[00391] 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00392] 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 multimeric polypeptide 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 multimeric polypeptide 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

[00393] The present disclosure provides a nucleic acid comprising nucleotide sequences encoding at least the first polypeptide and the second polypeptide of a multimeric polypeptide of the present disclosure. In some cases, where a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00394] 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00395] 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 β 2-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.

[00396] Suitable MHC polypeptides are described above. In some cases, the first MHC polypeptide is a β 2-microglobulin polypeptide; and wherein the second MHC polypeptide is an MHC class I heavy chain polypeptide. In some cases, the β 2-microglobulin polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to a β 2M 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. In some cases, the MHC class I heavy chain polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence depicted in any one of FIG. 3A-3C. In some cases, the first MHC polypeptide is an MHC Class II alpha chain polypeptide; and wherein the second MHC polypeptide is an MHC class II beta chain polypeptide.

[00397] 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 Figures 2A-2G.

[00398] Suitable immunomodulatory polypeptides are described above.

[00399] Suitable proteolytically cleavable linkers are described above. In some cases, the proteolytically cleavable linker comprises an amino acid sequence selected from: a) LEVLFGQP (SEQ ID NO:44); b) ENLYTQS (SEQ ID NO:45); c) DDDDK (SEQ ID NO:46); d) LVPR (SEQ ID NO:47); and e) GSGATNFSLLKQAGDVEENPGP (SEQ ID NO:48).

[00400] 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

[00401] 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.

[00402] 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 Ophthalmol Vis Sci 35:2543 2549, 1994; Borrás 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 Ophthalmol 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.

[00403] 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.

[00404] 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).

[00405] 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.

[00406] 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

[00407] The present disclosure provides a genetically modified host cell, where the host cell is genetically modified with a nucleic acid of the present disclosure.

[00408] 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. CCL1.3), human embryonic kidney (HEK) cells (ATCC No. CRL1573), HLHepG2 cells, and the like.

[00409] In some cases, the host cell is a mammalian cell that has been genetically modified such that it does not synthesize endogenous MHC β 2-M.

[00410] 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.

COMPOSITIONS

[00411] The present disclosure provides compositions, including pharmaceutical compositions, comprising TMMP (synTac) of the present disclosure. The present disclosure provides compositions, including pharmaceutical compositions, comprising a multimeric polypeptide 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

[00412] A composition of the present disclosure can comprise, in addition to a multimeric polypeptide of the present disclosure, one or more of: a salt, e.g., NaCl, MgCl₂, KCl, MgSO₄, 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.

[00413] 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.

[00414] A pharmaceutical composition can comprise a multimeric polypeptide 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.

[00415] 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.

[00416] 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.

[00417] Where a multimeric polypeptide 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

subject protein following administration. For example, the protein 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.

[00418] 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.

[00419] The concentration of a multimeric polypeptide 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.

[00420] 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.

[00421] 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 for the multimeric polypeptides. In some cases, the excipient is a pharmaceutically acceptable excipient.

[00422] In some cases, a T-cell multimeric polypeptide 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 T-cell multimeric polypeptide of the present disclosure. In some cases, a composition of the present disclosure comprises: a) a T-cell multimeric polypeptide 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 T-cell multimeric polypeptide 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

[00423] 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.

[00424] 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-hydroxyethylpiperazine-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, MgCl₂, KCl, MgSO₄, etc.

[00425] 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.

[00426] 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.

[00427] 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.

[00428] 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.

[00429] 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.

[00430] 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.

[00431] 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.

[00432] 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 minitables. 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, triethanolamine, N,N-dimethylacetamide, N,N-dimethylformamide, 2-pyrrolidone and derivatives thereof, tetrahydrofurfuryl alcohol, and AZONE™.

METHODS OF MODULATING T CELL ACTIVITY

[00433] 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 multimeric polypeptide of the present disclosure, where contacting the T cell with a multimeric polypeptide 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*.

[00434] In some cases, e.g., where the target T cell is a CD8⁺ T cell, the multimeric polypeptide comprises Class I MHC polypeptides (e.g., β 2-microglobulin and Class I MHC heavy chain). In some cases, e.g., where the target T cell is a CD4⁺ T cell, the multimeric polypeptide comprises Class II MHC polypeptides (e.g., Class II MHC α chain; Class II MHC β chain).

[00435] Where a multimeric polypeptide of the present disclosure includes an immunomodulatory polypeptide that is an activating polypeptide, contacting the T cell with the multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide increases the number of the epitope-specific T cells.

[00436] 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 multimeric polypeptide 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 multimeric polypeptide increases the number of the epitope-specific T cells.

[00437] Where a multimeric polypeptide of the present disclosure includes an immunomodulatory polypeptide that is an inhibiting polypeptide, contacting the T cell with the multimeric 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.

TREATMENT METHODS

[00438] 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 multimeric polypeptide 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.

[00439] 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.

[00440] 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.

[00441] 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 multimeric polypeptide of the present disclosure, or one or more nucleic acids (e.g., expression vectors; mRNA; etc.) comprising nucleotide sequences encoding the multimeric polypeptide, where the multimeric polypeptide 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 multimeric polypeptide of the present disclosure.

[00442] In some cases, the immunomodulatory polypeptide is an activating polypeptide, and the multimeric polypeptide activates the epitope-specific T cell. In some cases, the epitope is a cancer-associated epitope, and the multimeric polypeptide increases the activity of a T cell specific for the cancer-associated epitope.

[00443] The present disclosure provides a method of treating cancer in an individual, the method comprising administering to the individual an effective amount of a multimeric polypeptide of the present disclosure, or one or more nucleic acids (e.g., expression vectors; mRNA; etc.) comprising nucleotide sequences encoding the multimeric polypeptide, where the multimeric polypeptide comprises a T-cell epitope that is a cancer epitope, and where the multimeric polypeptide comprises a stimulatory immunomodulatory polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the multimeric polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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.

[00444] In some cases, an “effective amount” of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the multimeric polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the multimeric polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide.

[00445] 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 multimeric polypeptide 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 multimeric polypeptide increases the number of the epitope-specific T cells.

[00446] 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 multimeric polypeptide of the present disclosure, or one or more nucleic acids comprising nucleotide sequences encoding the multimeric polypeptide, where the multimeric polypeptide comprises a T-cell epitope that is a viral epitope, and where the multimeric polypeptide comprises a stimulatory immunomodulatory polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the multimeric polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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.

[00447] 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 multimeric polypeptide, where the multimeric polypeptide comprises a T-cell epitope that is a pathogen-associated epitope, and where the multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the multimeric polypeptide. In some cases, an “effective amount” of a multimeric polypeptide 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.

[00448] In some cases, the immunomodulatory polypeptide is an inhibitory polypeptide, and the multimeric polypeptide inhibits activity of the epitope-specific T cell. In some cases, the epitope is a self-epitope, and the multimeric polypeptide selectively inhibits the activity of a T cell specific for the self-epitope.

[00449] 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 multimeric polypeptide of the present disclosure, or one or more nucleic acids comprising nucleotide sequences encoding the multimeric polypeptide, where the multimeric polypeptide comprises a T-cell epitope that is a self epitope, and where the multimeric polypeptide 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 multimeric polypeptide, or in the absence of administration with the TMMP. In some cases, an “effective amount” of a multimeric polypeptide 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.

[00450] 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 multimeric polypeptide *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

[00451] Suitable formulations are described above, where suitable formulations include a pharmaceutically acceptable excipient. In some cases, a suitable formulation comprises: a) a T-cell modulatory multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00452] Suitable pharmaceutically acceptable excipients are described above.

Dosages

[00453] 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 multimeric polypeptide 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 multimeric polypeptide 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.

[00454] In some cases, a suitable dose of a multimeric polypeptide 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 multimeric polypeptide 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.

[00455] Those of skill will readily appreciate that dose levels can vary as a function of the specific multimeric polypeptide, 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.

[00456] In some cases, multiple doses of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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).

[00457] The duration of administration of a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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

[00458] An active agent (a multimeric polypeptide 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.

[00459] 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 multimeric polypeptide and/or the desired effect. A multimeric polypeptide 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.

[00460] In some cases, a multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide 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 multimeric polypeptide of the present disclosure, a nucleic acid of the present disclosure, or a recombinant expression vector of the present disclosure is administered subcutaneously.

[00461] In some cases, a multimeric polypeptide of the present disclosure is administered intravenously. In some cases, a multimeric polypeptide of the present disclosure is administered intramuscularly. In some cases, a multimeric polypeptide of the present disclosure is administered locally. In some cases, a multimeric polypeptide of the present disclosure is administered intratumorally. In some cases, a multimeric polypeptide of the present disclosure is administered peritumorally. In some cases, a multimeric polypeptide of the present disclosure is administered intracranially. In some cases, a multimeric polypeptide is administered subcutaneously. In some cases, a multimeric polypeptide of the present disclosure is administered intralymphatically.

[00462] A multimeric polypeptide 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.

[00463] 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 multimeric polypeptide 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.

Subjects suitable for treatment

[00464] 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

[00465] 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 1-134 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:

[00466] Aspect 1. A T-cell modulatory multimeric polypeptide, wherein the multimeric polypeptide is:

[00467] A) a heterodimer comprising: a) a first polypeptide comprising a first major histocompatibility complex (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, 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 immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold; or

[00468] 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,

[00469] 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,

[00470] 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; 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

[00471] wherein the first polypeptide or the second polypeptide optionally comprises an Ig Fc polypeptide or a non-Ig scaffold; or

[00472] C) a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) an epitope; ii) a first major histocompatibility complex (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 multimeric polypeptide 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

[00473] 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 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; 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.

- [00474]** Aspect 2. T-cell modulatory multimeric polypeptide of aspect 1, wherein the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 50% higher than the affinity with which it binds the second T cell.
- [00475]** Aspect 3. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 2-fold higher than the affinity with which it binds the second T cell.
- [00476]** Aspect 4. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 5-fold higher than the affinity with which it binds the second T cell.
- [00477]** Aspect 5. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the T-cell modulatory multimeric polypeptide binds to the first T cell with an affinity that is at least 10-fold higher than the affinity with which it binds the second T cell.
- [00478]** Aspect 6. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-7} M.
- [00479]** Aspect 7. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-6} M.
- [00480]** Aspect 8. The T-cell modulatory multimeric polypeptide of aspect 1, wherein the variant immunomodulatory polypeptide binds the co-immunomodulatory polypeptide with an affinity of from about 10^{-4} M to about 10^{-5} M.
- [00481]** Aspect 9. The T-cell modulatory multimeric polypeptide of aspect 1, 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.

[00482] Aspect 10. The T-cell modulatory multimeric polypeptide of aspect 1, 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 50:1.

[00483] Aspect 11. The T-cell modulatory multimeric polypeptide of aspect 1, 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 a T-cell modulatory multimeric polypeptide of the present disclosure comprising a variant of the wild-type immunomodulatory polypeptide to the cognate co-immunomodulatory polypeptide, when measured by bio-layer interferometry, is at least 10^2 :1.

[00484] Aspect 12. The T-cell modulatory multimeric polypeptide of aspect 1, 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 10^3 :1.

[00485] Aspect 13. The T-cell modulatory multimeric polypeptide of any one of aspects 1-12, wherein the second polypeptide comprises an Ig Fc polypeptide.

[00486] Aspect 14. The T-cell modulatory multimeric polypeptide of aspect 13, wherein the IgFc polypeptide is an IgG1 Fc polypeptide.

[00487] Aspect 15. The T-cell modulatory multimeric polypeptide of aspect 14, wherein the IgG1 Fc polypeptide comprises one or more amino acid substitutions selected from N297A, L234A, L235A, L234F, L235E, and P331S.

[00488] Aspect 16. The T-cell modulatory multimeric polypeptide of aspect 14, wherein the IgG1 Fc polypeptide comprises L234A and L235A substitutions.

- [00489]** Aspect 17. The T-cell modulatory multimeric polypeptide of any one of aspects 1-16, wherein the first polypeptide comprises a peptide linker between the epitope and the first MHC polypeptide.
- [00490]** Aspect 18. The T-cell modulatory multimeric polypeptide of aspect 17, wherein the linker has a length of from 20 amino acids to 40 amino acids.
- [00491]** Aspect 19. The T-cell modulatory multimeric polypeptide of aspect 17, wherein the linker is a peptide of the formula (GGGGS)_n, where n is 1, 2, 3, 4, 5, 6, 7, or 8.
- [00492]** Aspect 20. The T-cell modulatory multimeric polypeptide of any one of aspects 1-19, wherein the first polypeptide comprises a peptide linker between the variant immunomodulatory polypeptide and the second MHC polypeptide.
- [00493]** Aspect 21. The T-cell modulatory multimeric polypeptide of aspect 18, wherein the linker has a length of from 20 amino acids to 40 amino acids.
- [00494]** Aspect 22. The T-cell modulatory multimeric polypeptide of aspect 20, wherein the linker is a peptide of the formula (GGGGS)_n, where n is 1, 2, 3, 4, 5, 6, 7, or 8.
- [00495]** Aspect 23. The T-cell modulatory multimeric polypeptide of any one of aspects 1-22, comprising two or more copies of the variant immunomodulatory polypeptide.
- [00496]** Aspect 24. The T-cell modulatory multimeric polypeptide of aspect 23, wherein the two or more copies of the variant immunomodulatory polypeptide comprise the same amino acid sequence.
- [00497]** Aspect 25. The T-cell modulatory multimeric polypeptide of aspect 23 or aspect 24, comprising a peptide linker between the copies.
- [00498]** Aspect 26. The T-cell modulatory multimeric polypeptide of aspect 25, wherein the linker has a length of from 20 amino acids to 40 amino acids.
- [00499]** Aspect 27. The T-cell modulatory multimeric polypeptide of aspect 25, wherein the linker is a peptide of the formula (GGGGS)_n, where n is 1, 2, 3, 4, 5, 6, 7, or 8.
- [00500]** Aspect 28. The T-cell modulatory multimeric polypeptide of any one of aspects 1-27, wherein the variant immunomodulatory polypeptide comprises from 1 to 10 amino acid substitutions relative to a corresponding wild-type immunomodulatory polypeptide.
- [00501]** Aspect 29. The T-cell modulatory multimeric polypeptide of aspect 28, wherein the wild-type immunomodulatory polypeptide is selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM.
- [00502]** Aspect 30. The T-cell modulatory multimeric polypeptide of any one of aspects 1-29, wherein the first MHC polypeptide is a β 2-microglobulin polypeptide; and wherein the second MHC polypeptide is an MHC class I heavy chain polypeptide.

- [00503]** Aspect 31. The T-cell modulatory multimeric polypeptide of aspect 30, wherein the β 2-microglobulin polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to one of the amino acid sequences set forth in FIG. 4.
- [00504]** Aspect 32. The T-cell modulatory multimeric polypeptide of aspect 30, wherein the MHC class I heavy chain polypeptide is an HLA-A, an HLA-B, or an HLA-C heavy chain.
- [00505]** Aspect 33. The T-cell modulatory multimeric polypeptide of aspect 32, wherein the MHC class I heavy chain polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence set forth in one of FIG. 3A-3C.
- [00506]** Aspect 34. The T-cell modulatory multimeric polypeptide of any one of aspects 1-29, wherein the first MHC polypeptide is an MHC Class II alpha chain polypeptide; and wherein the second MHC polypeptide is an MHC class II beta chain polypeptide.
- [00507]** Aspect 35. The T-cell modulatory multimeric polypeptide of any one of aspects 1-34, wherein multimeric polypeptide comprises an Fc polypeptide, and wherein 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.
- [00508]** Aspect 36. The T-cell modulatory multimeric polypeptide of aspect 26, wherein the Ig Fc polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to an amino acid sequence depicted in one of FIG. 2A-2D.
- [00509]** Aspect 37. The T-cell modulatory multimeric polypeptide of aspect 35 or 36, wherein the second polypeptide comprises a peptide linker between second MHC polypeptide and the Fc polypeptide.
- [00510]** Aspect 38. The T-cell modulatory multimeric polypeptide of aspect 37, wherein the linker has a length of from 20 amino acids to 4 amino acids.
- [00511]** Aspect 39. The T-cell modulatory multimeric polypeptide of aspect 37, wherein the linker is a peptide of the formula (GGGS)_n, where n is 1, 2, 3, 4, 5, 6, 7, or 8.
- [00512]** Aspect 40. The T-cell modulatory multimeric polypeptide of any one of aspects 1-39, wherein the first polypeptide and the second polypeptide are non-covalently associated.
- [00513]** Aspect 41. The T-cell modulatory multimeric polypeptide of any one of aspects 1-39, wherein the first polypeptide and the second polypeptide are covalently linked to one another.
- [00514]** Aspect 42. The T-cell modulatory multimeric polypeptide of aspect 41, wherein the covalent linkage is via a disulfide bond.

- [00515]** Aspect 43. The T-cell modulatory multimeric polypeptide of aspect 42, wherein the disulfide bond links a cysteine residue in the first MHC polypeptide with a cysteine residue in the second MHC polypeptide.
- [00516]** Aspect 44. The T-cell modulatory multimeric polypeptide of any one of aspects 1-43, wherein the epitope is a cancer epitope.
- [00517]** Aspect 45. The T-cell modulatory multimeric polypeptide of aspect 44, wherein the cancer epitope is a peptide fragment 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, or 20 aa in length of a MUC1 polypeptide, a human papillomavirus (HPV) E6 polypeptide, an LMP2 polypeptide, an HPV E7 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 alpha-fetoprotein (AFP) 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 (PDGF β) polypeptide, a MAD-CT-2 polypeptide, a Fos-related antigen-1 (FOSL) polypeptide, or a Wilms tumor-1 (WT1) polypeptide.

- [00518]** Aspect 46. The T-cell modulatory multimeric polypeptide of any one of aspects 1-45, wherein one of the first and the second polypeptide comprises an Ig Fc polypeptide, wherein a drug is conjugated to the Ig Fc polypeptide.
- [00519]** Aspect 47. The T-cell modulatory multimeric polypeptide of aspect 46, wherein 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 leptomyacin, or a pro-drug of any one of the foregoing.
- [00520]** Aspect 48. The T-cell modulatory multimeric polypeptide of aspect 46, wherein the drug is a retinoid.
- [00521]** Aspect 49. The T-cell modulatory multimeric polypeptide of any one of aspects 1-48, wherein the binding affinity is determined by bio-layer interferometry.
- [00522]** Aspect 50. 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 1-49, 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.
- [00523]** Aspect 51. The method of aspect 50, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 5:1.
- [00524]** Aspect 52. The method of aspect 50, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 10:1.
- [00525]** Aspect 53. The method of aspect 50, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 25:1.

- [00526]** Aspect 54. The method of aspect 50, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 50:1.
- [00527]** Aspect 55. The method of aspect 50, wherein the ratio of the epitope-specific T cell response to the epitope-non-specific T cell response is at least 100:1.
- [00528]** Aspect 56. The method of any one of aspects 50-55, wherein the individual is a human.
- [00529]** Aspect 57. The method of any one of aspects 50-56, wherein said modulating comprises increasing a cytotoxic T-cell response to a cancer cell.
- [00530]** Aspect 58. The method of any one of aspects 50-57, wherein said modulating comprises reducing a T-cell response to an autoantigen.
- [00531]** Aspect 59. The method of any one of aspects 50-58, wherein said administering is intravenous, subcutaneous, intramuscular, systemic, intralymphatic, distal to a treatment site, local, or at or near a treatment site.
- [00532]** Aspect 60. The method of any one of aspects 50-59, 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.
- [00533]** Aspect 61. A method of treating cancer in an individual, the method comprising administering to the individual an effective amount of a T-cell modulatory multimeric polypeptide of any one of aspects 1-49.
- [00534]** Aspect 62. One or more nucleic acids comprising nucleotide sequences encoding the first and the second polypeptide of the T-cell modulatory multimeric polypeptide of any one of aspects 1-49.
- [00535]** Aspect 63. The one or more nucleic acids of aspect 62, wherein the first polypeptide is encoded by a first nucleotide sequence, the second polypeptide is encoded by a second nucleotide sequence, and wherein the first and the second nucleotide sequences are present in a single nucleic acid.
- [00536]** Aspect 64. The one or more nucleic acids of aspect 62, wherein the first polypeptide is encoded by a first nucleotide sequence present in a first nucleic acid, and the second polypeptide is encoded by a second nucleotide sequence present in a second nucleic acid.
- [00537]** Aspect 65. The one or more nucleic acids of aspect 63, wherein the first nucleotide sequence and the second nucleotide sequence are operably linked to a transcriptional control element.

- [00538]** Aspect 66. The one or more nucleic acids of aspect 64, wherein the first nucleotide sequence is operably linked to a transcriptional control element and the second nucleotide sequence is operably linked to a transcriptional control element.
- [00539]** Aspect 67. The one or more nucleic acids of aspect 63, wherein the single nucleic acid is present in a recombinant expression vector.
- [00540]** Aspect 68. The one or more nucleic acids of aspect 67, wherein the first nucleic acid is present in a first recombinant expression vector and the second nucleic acid is present in a second recombinant expression vector.
- [00541]** Aspect 69. A composition comprising: a) the T-cell modulatory multimeric polypeptide of any one of aspects 1-49; and b) a pharmaceutically acceptable excipient.
- [00542]** Aspect 70. A composition comprising: a) the one or more nucleic acids of any one of aspects 62-68; and b) a pharmaceutically acceptable excipient.
- [00543]** Aspect 71. A composition comprising: a) the T-cell modulatory multimeric polypeptide of any one of aspects 1-49; and b) saline.
- [00544]** Aspect 72. The composition of aspect 71, wherein the saline is 0.9% NaCl.
- [00545]** Aspect 73. The composition of aspect 71 or 72, wherein the composition is sterile.
- [00546]** Aspect 74. A method of obtaining a T-cell modulatory multimeric polypeptide 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 T-cell modulatory multimeric polypeptides 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 major histocompatibility complex (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 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.
- [00547]** Aspect 75. A method of obtaining a T-cell modulatory multimeric polypeptide 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 T-cell

modulatory multimeric polypeptides comprising a plurality of members, wherein the plurality of member comprises: a) a first polypeptide comprising: i) an epitope; and ii) a first major histocompatibility complex (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 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.

[00548] Aspect 76. The method of aspect 74 or 75, wherein said selecting comprises determining the affinity, using bio-layer interferometry, of binding between T-cell modulatory multimeric polypeptide library members and the cognate co-immunomodulatory polypeptide.

[00549] Aspect 77. The method of any one of aspects 74-76, wherein the T-cell modulatory multimeric polypeptide is as defined in any one of aspects 1-49.

[00550] Aspect 78. The method of any one of aspects 74-77, further comprising: a) contacting the selected T-cell modulatory multimeric polypeptide 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 T-cell modulatory multimeric polypeptide library member comprises an epitope tag, such that the T-cell modulatory multimeric polypeptide library member binds to the target T-cell; b) contacting the selected T-cell modulatory multimeric polypeptide library member bound to the target T-cell with a fluorescently labeled binding agent that binds to the epitope tag, generating a selected T-cell modulatory multimeric polypeptide library member/target T-cell/binding agent complex; and c) measuring the mean fluorescence intensity (MFI) of the selected T-cell modulatory multimeric polypeptide library member/target T-cell/binding agent complex using flow cytometry, wherein the MFI measured over a range of concentrations of the selected T-cell modulatory multimeric polypeptide library member provides a measure of the affinity and apparent avidity; wherein a selected T-cell modulatory multimeric polypeptide library member that selectively binds the target T cell, compared to binding of the T-cell modulatory multimeric polypeptide 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 T-cell modulatory multimeric polypeptide library member, is identified as selectively binding to the target T cell.

- [00551]** Aspect 79. The method of aspect 78, wherein the binding agent is an antibody specific for the epitope tag.
- [00552]** Aspect 80. The method of any one of aspects 74-79, wherein the variant immunomodulatory polypeptide comprises from 1 to 20, amino acid substitutions compared to the corresponding parental wild-type immunomodulatory polypeptide.
- [00553]** Aspect 81. The method of any one of aspects 74-80, wherein the T-cell modulatory multimeric polypeptide comprises two variant immunomodulatory polypeptides.
- [00554]** Aspect 82. The method of aspect 81, wherein the two variant immunomodulatory polypeptides comprise the same amino acid sequence.
- [00555]** Aspect 83. The method of aspect 81 or 82, wherein 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.
- [00556]** Aspect 84. The method of aspect 81 or 82, wherein the two variant immunomodulatory polypeptides are on the same polypeptide chain of the T-cell modulatory multimeric polypeptide.
- [00557]** Aspect 85. The method of aspect 84, wherein the two variant immunomodulatory polypeptides are on the first polypeptide of the T-cell modulatory multimeric polypeptide.
- [00558]** Aspect 86. The method of aspect 84, wherein the two variant immunomodulatory polypeptides are on the second polypeptide of the T-cell modulatory multimeric polypeptide.
- [00559]** Aspect 87. The method of any one of aspects 74-86, further comprising isolating the selected T-cell modulatory multimeric polypeptide library member from the library.
- [00560]** Aspect 88. The method of any one of aspects 74-87, further comprising providing a nucleic acid comprising a nucleotide sequence encoding the selected T-cell modulatory multimeric polypeptide library member.
- [00561]** Aspect 89. The method of aspect 88, wherein the nucleic acid is present in a recombinant expression vector.
- [00562]** Aspect 90. The method of aspect 88 or 89, wherein the nucleotide sequence is operably linked to a transcriptional control element that is functional in a eukaryotic cell.
- [00563]** Aspect 91. The method of any one of aspects 88-90, further comprising introducing the nucleic acid into a eukaryotic host cell, and culturing the cell in a liquid medium to

synthesize the encoded selected T-cell modulatory multimeric polypeptide library member in the cell.

[00564] Aspect 92. The method of aspect 91, further comprising isolating the synthesized selected T-cell modulatory multimeric polypeptide library member from the cell or from liquid culture medium comprising the cell.

[00565] Aspect 93. The method of any one of aspects 74-92, wherein the selected T-cell modulatory multimeric polypeptide library member comprises an Ig Fc polypeptide.

[00566] Aspect 94. The method of aspect 93, further comprising conjugating a drug to the Ig Fc polypeptide.

[00567] Aspect 95. The method of aspect 94, wherein 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.

[00568] Aspect 96. The method of aspect 94, wherein the drug is a retinoid.

[00569] Aspect 97. The method of any one of aspects 74-96, wherein 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; FasL and Fas; TGF β and TGF β receptor; CD80 and CD28; CD86 and CD28; OX40L and OX40; CD70 and CD27; ICOS-L and ICOS; ICAM and LFA-1; JAG1 and Notch; JAG1 and CD46; CD80 and CTLA4; and CD86 and CTLA4.

[00570] Aspect 98. A multimeric T-cell modulatory polypeptide comprising: A) a first multimeric polypeptide heterodimer according to any of aspects 1-49, and B) a second multimeric polypeptide heterodimer according to any of aspects 1-49, and wherein the first heterodimer and the second heterodimer are covalently linked to one another.

[00571] Aspect 99. The multimeric T-cell modulatory polypeptide of aspect 98, wherein 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.

[00572] Aspect 100. The multimeric T-cell modulatory polypeptide of aspect 98 or 99, wherein the peptide epitope of the first heterodimer and the peptide epitope of the second heterodimer comprise the same amino acid sequence.

[00573] Aspect 101. The multimeric T-cell modulatory polypeptide of any one of aspects 98-100, wherein the first MHC polypeptide of the first and the second heterodimer is an

MHC Class I β 2-microglobulin, and wherein the second MHC polypeptide of the first and the second heterodimer is an MHC Class I heavy chain.

- [00574]** Aspect 102. The multimeric T-cell modulatory polypeptide of any one of aspects 98-101, wherein the one or more immunomodulatory polypeptides of the first heterodimer and the one or more immunomodulatory polypeptides of the second heterodimer comprise the same amino acid sequence or comprise different amino acid sequences.
- [00575]** Aspect 103. The multimeric T-cell modulatory polypeptide of any one of aspects 98-102, wherein the one or more immunomodulatory polypeptides of the first heterodimer and the one or more immunomodulatory polypeptides 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.
- [00576]** Aspect 104. The multimeric T-cell modulatory polypeptide of any one of aspects 98-103, wherein the one or more immunomodulatory polypeptides of the first heterodimer and the one or more immunomodulatory polypeptides of the second heterodimer are selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, ICAM, variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and combinations thereof.
- [00577]** Aspect 105. The multimeric T-cell modulatory polypeptide of aspect 104, wherein 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; FasL and Fas; TGF β and TGF β receptor; CD80 and CD28; CD86 and CD28; OX40L and OX40; CD70 and CD27; ICOS-L and ICOS; ICAM and LFA-1; JAG1 and Notch; JAG1 and CD46; CD80 and CTLA4; and CD86 and CTLA4.
- [00578]** Aspect 106. The multimeric T-cell modulatory polypeptide of any one of aspects 98-105, wherein the peptide epitope is a cancer epitope.
- [00579]** Aspect 107. The multimeric T-cell modulatory polypeptide of aspect 106, wherein the cancer epitope is a peptide fragment 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, or 20 aa in length of a MUC1 polypeptide, a human papillomavirus (HPV) E6 polypeptide, an LMP2 polypeptide, an HPV E7 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 alpha-fetoprotein (AFP) 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 (PDGF β) polypeptide, a MAD-CT-2 polypeptide, a Fos-related antigen-1 (FOSL) polypeptide, or a Wilms tumor-1 (WT1) polypeptide.

- [00580]** Aspect 108. 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 multimeric polypeptide of any one of aspects 1-49 and 98-107, 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 multimeric polypeptide, and wherein said contacting delivers the one or more costimulatory polypeptides present within the multimeric polypeptide to the target T cell.
- [00581]** Aspect 109. The method of aspect 108, wherein the population of T cells is *in vitro*.
- [00582]** Aspect 110. The method of aspect 108, wherein the population of T cells is *in vivo* in an individual.
- [00583]** Aspect 111. The method of aspect 110, comprising administering the multimeric polypeptide to the individual.
- [00584]** Aspect 112. The method of any one of aspects 108-111, wherein the target T cell is a regulatory T cell.
- [00585]** Aspect 113. The method of any one of aspects 108-111, wherein the target T cell is a cytotoxic T cell.
- [00586]** Aspect 114. The method of aspect 108, 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.
- [00587]** Aspect 115. The method of aspect 114, further comprising administering the population of activated and/or proliferated target T cells to the individual.
- [00588]** Aspect 116. 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 the multimeric polypeptide of any one of aspects 1-49 and 98-107, wherein the multimeric polypeptide 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.
- [00589]** Aspect 117. The method of aspects 108-115, wherein the one or more costimulatory polypeptides of the first heterodimer are selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, ICAM, variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and combinations thereof, and

- [00590]** wherein the one or more costimulatory polypeptides of the second heterodimer are selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, ICAM, variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and combinations thereof.
- [00591]** Aspect 118. The method of aspect 117, wherein the one or more costimulatory polypeptides of the first heterodimer are selected from the group consisting of IL-2, a variant of IL-2, and combinations thereof, and the one or more costimulatory polypeptides of the second heterodimer are selected from the group consisting of IL-2, a variant of IL-2, and combinations thereof.
- [00592]** Aspect 119. The method of aspect 117, wherein the one or more costimulatory polypeptides of the first heterodimer are selected from the group consisting of 4-1BBL, a variant of 4-1BBL, and combinations thereof, and the one or more costimulatory polypeptides of the second heterodimer are selected from the group consisting of 4-1BBL, a variant of 4-1BBL, and combinations thereof.
- [00593]** Aspect 120. The method of aspect 117, wherein the one or more costimulatory polypeptides of the first heterodimer are selected from the group consisting of CD80, a variant of CD80, and combinations thereof, and the one or more costimulatory polypeptides of the second heterodimer are selected from the group consisting of CD80, a variant of CD80, and combinations thereof.
- [00594]** Aspect 121. The method of aspect 117, wherein the first heterodimer comprises at least two costimulatory polypeptides that are each independently selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and
- [00595]** wherein the second heterodimer comprises at least two costimulatory polypeptides that are each independently selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM.
- [00596]** Aspect 122. The method of aspect 121, wherein each of the at least two costimulatory polypeptides of the first heterodimer is independently selected from the group consisting of IL-2 and variants of IL-2, and each of the at least two costimulatory polypeptides of the second heterodimer is independently selected from the group consisting of IL-2 and variants of IL-2.

- [00597]** Aspect 123. The method of aspect 121, wherein each of the at least two costimulatory polypeptides of the first heterodimer is independently selected from the group consisting of 4-1BBL and variants of 4-1BBL, and each of the at least two costimulatory polypeptides of the second heterodimer is independently selected from the group consisting of 4-1BBL and variants of 4-1BBL.
- [00598]** Aspect 124. The method of aspect 121, wherein each of the at least two costimulatory polypeptides of the first heterodimer is independently selected from the group consisting of CD80 and variants of CD80, and each of the at least two costimulatory polypeptides of the second heterodimer is independently selected from the group consisting of CD80 and variants of CD80.
- [00599]** Aspect 125. The method of aspect 121, wherein at least one of the at least two costimulatory polypeptides of the first heterodimer is CD80 or a variant of CD80, and at least one of the at least two costimulatory polypeptides of the first heterodimer is 4-1BBL or a variant of 4-1BBL, and
- [00600]** wherein at least one of the at least two costimulatory polypeptides of the second heterodimer is CD80 or a variant of CD80, and at least one of the at least two costimulatory polypeptides of the second heterodimer is 4-1BBL or a variant of 4-1BBL.
- [00601]** Aspect 126. The multimeric T-cell modulatory polypeptide of any one of aspects 98-107, wherein the one or more immunomodulatory (i.e., costimulatory) polypeptides of the first heterodimer are selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and combinations thereof, and
- [00602]** wherein the one or more immunomodulatory (i.e., costimulatory) polypeptides of the second heterodimer are selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and combinations thereof.
- [00603]** Aspect 127. The multimeric T-cell modulatory polypeptide of aspect 126, wherein the one or more immunomodulatory polypeptides of the first heterodimer are selected from the group consisting of IL-2, a variant of IL-2, and combinations thereof, and the one or more immunomodulatory polypeptides of the second heterodimer are selected from the group consisting of IL-2, a variant of IL-2, and combinations thereof.

- [00604]** Aspect 128. The multimeric T-cell modulatory polypeptide of aspect 126, wherein the one or more immunomodulatory polypeptides of the first heterodimer are selected from the group consisting of 4-1BBL, a variant of 4-1BBL, and combinations thereof, and the one or more immunomodulatory polypeptides of the second heterodimer are selected from the group consisting of 4-1BBL, a variant of 4-1BBL, and combinations thereof.
- [00605]** Aspect 129. The multimeric T-cell modulatory polypeptide of aspect 126, wherein the one or more immunomodulatory polypeptides of the first heterodimer are selected from the group consisting of CD80, a variant of CD80, and combinations thereof, and the one or more immunomodulatory polypeptides of the second heterodimer are selected from the group consisting of CD80, a variant of CD80, and combinations thereof.
- [00606]** Aspect 130. The multimeric T-cell modulatory polypeptide of aspect 126, wherein the first heterodimer comprises at least two immunomodulatory polypeptides that are each independently selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, , ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and
- [00607]** wherein the second heterodimer comprises at least two immunomodulatory polypeptides that are each independently selected from the group consisting of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM, and variants of IL-2, 4-1BBL, PD-L1, CD80, CD86, ICOS-L, OX-40L, FasL, JAG1, TGF β , CD70, and ICAM.
- [00608]** Aspect 131. The multimeric T-cell modulatory polypeptide of aspect 130, wherein each of the at least two immunomodulatory polypeptides of the first heterodimer is independently selected from the group consisting of IL-2 and variants of IL-2, and each of the at least two immunomodulatory polypeptides of the second heterodimer is independently selected from the group consisting of IL-2 and a variant of IL-2.
- [00609]** Aspect 132. The multimeric T-cell modulatory polypeptide of aspect 130, wherein each of the at least two immunomodulatory polypeptides of the first heterodimer is independently selected from the group consisting of 4-1BBL and variants of 4-1BBL, and each of the at least two immunomodulatory polypeptides of the second heterodimer is independently selected from the group consisting of 4-1BBL and variants of 4-1BBL.
- [00610]** Aspect 133. The multimeric T-cell modulatory polypeptide of aspect 130, wherein each of the at least two immunomodulatory polypeptides of the first heterodimer is independently selected from the group consisting of CD80 and variants of CD80, and

each of the at least two immunomodulatory polypeptides of the second heterodimer is independently selected from the group consisting of CD80 and variants of CD80.

[00611] Aspect 134. The multimeric T-cell modulatory polypeptide of aspect 130, wherein at least one of the at least two immunomodulatory polypeptides of the first heterodimer is CD80 or a variant of CD80, and at least one of the at least two immunomodulatory polypeptides of the first heterodimer is 4-1BBL or a variant of 4-1BBL, and wherein at least one of the at least two immunomodulatory polypeptides of the second heterodimer is CD80 or a variant of CD80, and at least one of the at least two immunomodulatory polypeptides of the second heterodimer is 4-1BBL or a variant of 4-1BBL.

[00612] 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 (TMMP) comprising:
at least one heterodimer comprising:
 - a) a first polypeptide comprising:
 - i) a Wilms tumor-1 (WT-1) peptide epitope, wherein the WT-1 peptide has a length of from 4 amino acids to 20 amino acids; and;
 - ii) a first class I major histocompatibility complex (MHC) polypeptide, wherein the first MHC polypeptide is a β 2 microglobulin (β 2M) polypeptide;
 - b) a second polypeptide comprising a second class I MHC polypeptide, wherein the second class I MHC polypeptide is a class I MHC heavy chain polypeptide; and
 - c) two immunomodulatory polypeptides, wherein the first and/or the second polypeptide comprises the two immunomodulatory polypeptides,
wherein the two immunomodulatory polypeptides each comprise a variant interleukin-2 (IL-2) polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:15, and having one or more amino acid substitutions relative to the amino acid sequence set forth in SEQ ID NO:15,
wherein the variant IL-2 polypeptides bind to IL-2 receptor (IL-2R) and exhibit reduced binding affinity to human wild-type IL-2R compared to the binding affinity of a control IL-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:15 for the IL-2R polypeptide when assayed under the same conditions in a bio-layer interferometry (BLI) assay.
2. The TMMP of claim 1, wherein the TMMP comprises an immunoglobulin (Ig) Fc polypeptide or a non-Ig scaffold.
3. A TMMP of claim 1, wherein:
 - a1) the first polypeptide comprises, in order from N-terminus to C-terminus:
 - i) the WT-1 peptide epitope;
 - ii) an optional linker; and
 - iii) a β 2M polypeptide; and
 - b1) the second polypeptide comprises, in order from N-terminus to C-terminus:

- i) the first reduced affinity IL-2 variant polypeptide.
- ii) an optional linker;
- iii) the second reduced affinity IL-2 variant polypeptide;
- iv) an optional linker;
- v) an MHC heavy chain polypeptide;
- vi) an optional linker; and
- vii) a variant Ig Fc polypeptide.

4. A TMMP of claim 1, wherein:

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

- i) the WT-1 peptide epitope;
- ii) an optional linker; and
- iii) a β 2M polypeptide; and

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

- i) an MHC heavy polypeptide;
- ii) an optional linker;
- iii) a variant Ig Fc polypeptide;
- iv) an optional linker;
- v) the first reduced affinity IL-2 variant polypeptide;
- vi) an optional linker;
- vii) the second reduced affinity IL-2 variant polypeptide.

5. A TMMP of any one of claims 1-4, wherein the MHC class I heavy chain polypeptide comprises an HLA-A heavy chain amino acid sequence, optionally having at least 85% amino acid sequence identity to an HLA-A heavy chain sequence set forth in SEQ ID NO. 53.

6. A TMMP according to any one of claims 1-5, wherein the at least one reduced affinity IL-2 variant polypeptide comprises the amino acid sequence of SEQ. ID NO: 15 having from 1-10 amino acid substitutions.

7. A TMMP according to any one of claims 1-6, wherein the at least one reduced affinity IL-2 variant polypeptide comprises the amino acid sequence of SEQ. ID NO: 25,

where X1 is any amino acid other than His, and where X2 is any amino acid other than Phe, optionally wherein X1 is Ala, X2 is Ala, or X1 is Ala and X2 is Ala.

8. A TMMP according to claim 7, wherein the at least one reduced affinity IL-2 variant polypeptide comprises Ala at residues 16 and 42.

9. A TMMP of any of one of claims 1-8, wherein the TMMP comprises a disulfide bond between a Cys residue in the β 2M polypeptide and a Cys residue in the MHC Class I heavy chain polypeptide.

10. A TMMP of any of one of claims 1-9, wherein the TMMP comprises a disulfide bond between a Cys residue at position 12 in the β 2M polypeptide and a Cys residue at position 236 in the MHC Class I heavy chain polypeptide.

11. A TMMP of any one of claims 1-8, wherein the first polypeptide comprises a Cys-containing linker between the epitope and the β 2M polypeptide, and wherein the TMMP comprises a disulfide bond between the Cys in the Cys-containing linker and a Cys in the MHC heavy chain.

12. A TMMP of any one of claims 2-11, wherein the Ig Fc polypeptide comprises 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 any one of SEQ ID NO:204 – SEQ ID NO:215.

13. A TMMP of any one of claims 2-12, wherein the Ig Fc polypeptide comprises a variant of a human IgG1 Fc polypeptide, optionally comprising at least about 95%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in any one of SEQ ID NO:204 – SEQ ID NO:215, optionally wherein the Ig Fc polypeptide comprises the amino acid sequence of SEQ ID NO:215.

14. A TMMP comprising a first and second heterodimer according to any one of claims 2-13, wherein the first and second heterodimers are the same and are covalently bonded to each other by one or more disulfide bonds between the Ig Fc polypeptides of the first and second heterodimers.

15. A pharmaceutical composition comprising a TMMP of any one of claims 1-14.
16. A composition comprising one or more nucleic acids comprising nucleotide sequences encoding the first and second polypeptides according to any one of claims 1-14.
17. A composition comprising one or more expression vectors, wherein the one or more expression vectors comprise nucleotide sequences encoding the first and second polypeptides according to any one of claims 1-14.
18. A host cell transformed with a composition of claim 16 or 17.
19. A method of selectively modulating the activity of T cell in vitro comprising contacting the T cell with a TMMP according to any one of claims 1-14.
20. A method of treating a cancer expressing a WT-1 epitope, comprising administering to an individual in need thereof a TMMP of any one of claims 1-14 or a pharmaceutical composition of claim 15.
21. A method of producing a TMMP of any one of claims 1 to 14, the method comprising culturing a host cell that is genetically modified with one or more expression vectors comprising nucleotide sequences encoding the first and the second polypeptides of the multimeric polypeptide, under conditions such that the genetically modified host cell produces the TMMP.
22. Use of a TMMP of any one of claims 1-14 in the manufacture of a medicament for treating a cancer expressing a WT-1 epitope.

FIG. 1

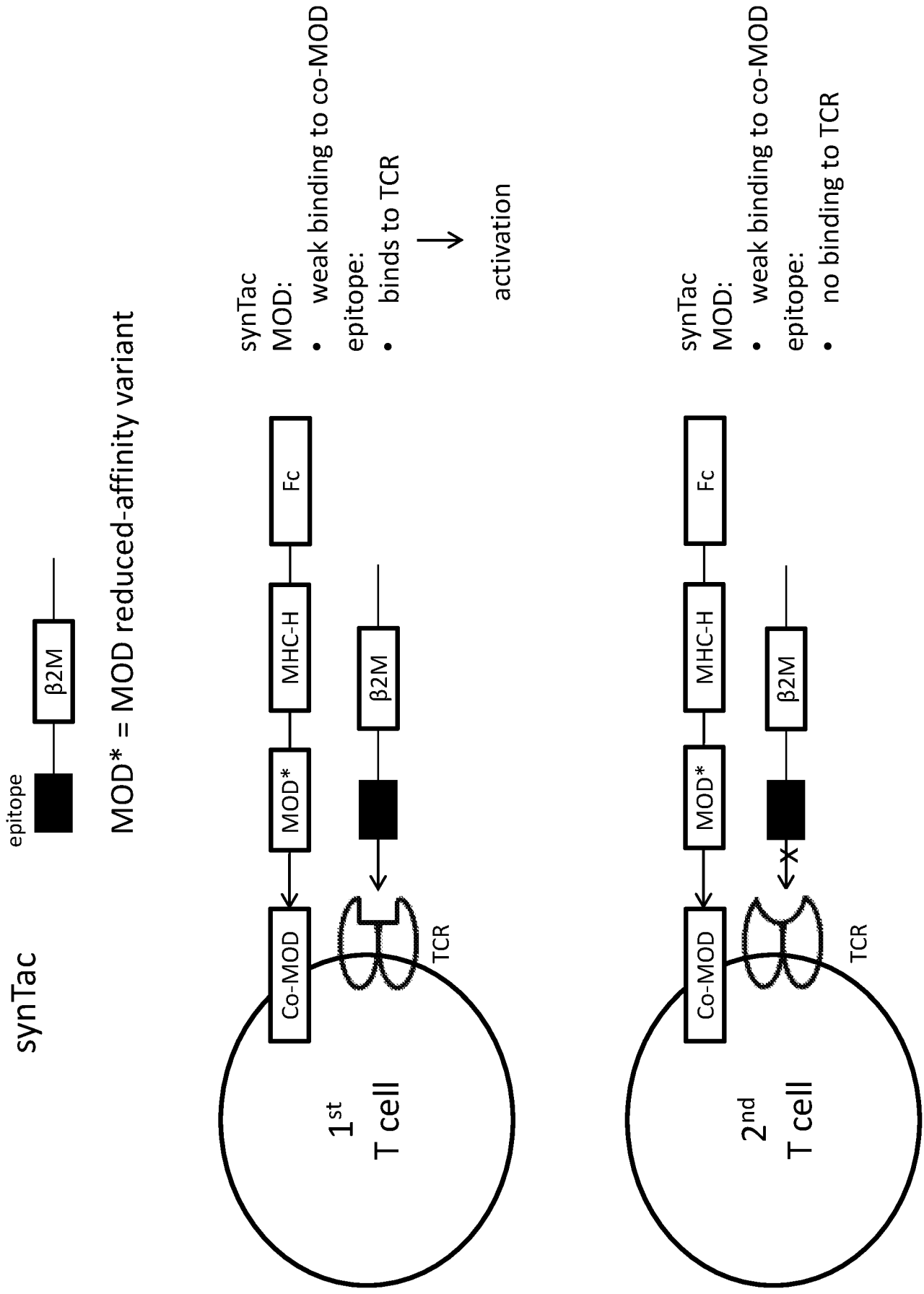


Figure 2A

GenBank 3S7G_A

Homo sapiens **IgG1 Fc** (SEQ ID NO:204)

227 aa

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1 dkthtcppcp apellggpsv flfppkpkdt lmisrtpevt cvvvdvshed pevknwyvd
61 gvevhnaktk preeqynsty rvsvltvlh qdwlngkeyk ckvsnkappa piektiskak
121 gqprepvyt lppsrdeltk nqsltcclvk gfypsdiave wesngqpenn ykttppvlds
181 dgsfflyskl tvdksrwqgg nvfscsvmhe alnhhtqks lslspgk

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GenBank AAN76044

Homo sapiens **IgG2 Fc** (amino acids 99-325) (SEQ ID NO:205)

227 aa

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1 stkgpsvfpl apcsrstses taalgcclvkd yfpepvtvsw nsgaltsgvh tfpavlqssg
61 lyslssvvtv pssnfgtqty tcnvdhkpsn tkvdktverk ccvecppcpa ppvagpsvfl
121 fppkpkdtlm isrtpevtcv vvdvshedpe vqfnwyvdgv evhnaktkpr eeqfnstfrv
181 vsvltvvhqd wlngkeykck vsnkglpapi ektisktgq prepqvvtlp psreemtknq
241 vsltcclvkgf ypsdiavewe snggpennnyk ttpmldsdg sfflyskltv dksrwqqgnv
301 fscsvmhcal hnhytqksls lspgk

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GenBank AAW65947

Homo sapiens **IgG3 Fc** (amino acids 19-246) (SEQ ID NO:206)

238 aa

```

1 hkpsntkvdk rvelktplgd tthtcppcpa pellggpsvf lfppkpkdtl misrtpevtc
61 vvvdvshedp evkfnwyvdg vevhnaktkp reeqynstyr vsvltvlhq dwlngkeykc
121 kvsnkalpap iektiskakg qprepvytl ppsrdeltkn qvsltcclvk gfypsdiavew
181 esngqpenny kttppvldsd gsfflysklt vdksrwqqgn vfscsvmhea lnhhtqksl
241 slspgk

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Figure 2B

GenBank AAA52770

Homo sapiens IgD Fc (amino acids 162-383) (SEQ ID NO:207)
222 aa

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1  ptkapdvfpi isgcrhpkdn spvvlacilit gyhptsvtvt wymgtqspq rtfpeiqrdd
61  syymtssqls tplqqwrqge ykcvvqhtas kskkeifrwsp espkaqassv ptaqpqaegs
121 lakattapat trntgrggee kkekekeeq eeretktpes pshtqplgvy lltpavqdlw
181 lrdkatftcf vvgddlkdah ltwevagkvp tggveeglle rhtngsqsqh srltlprslw
241 nagtsvtctl nhpslppqrl malrepaaqa pvklslnlla ssdppeaasw llcevsgfsp
301 pnillmwled grevntsgfa parppppqprs ttfwawsvlr vpappspqpa tytcvvhshed
361 srltlnasrs levsyytdhg pmk

```

GenBank 0308221A

Homo sapiens IgM Fc (SEQ ID NO:208)
276 aa

```

1  vtstltikzs dwlgesmftc rvdhrgltfq qnassmcpvd qdtairvfai ppsfasiflt
61  kstkltclvt dltybsvti swtreengav kthtnishes pnatfsavge asicedbdws
121 gerftctvth tdlpsplkqt isrpkgvalh rpbvylppa rzzlnlresa titclvtgfs
181 padvfvevmq rgeplspqky vtsapmpepq apgryfahsi ltvseeewnt ggtytcvvhah
241 ealpnrvter tvdkstgkpt lynvslvmsd tagtcy

```

Figure 2C

GenBank P01876	
<i>Homo sapiens</i> IgA Fc (amino acids 120-353) (SEQ ID NO:209)	
234 aa	
	1 asptspkvfp lslcstqpdg nvviaclvqg ffpqeplsvt wsesggqvta rnfppsqdas
	61 gdltyttssql tlpatqclag ksvtchvkhy tnpsqdvtpv cpvpstpptp spstpptpsp
	121 scchprlslh rpaledlllg seanltctlt glrdasgvtf twtpssgksa vggpperdlc
	181 gcysvssvlp gcaepwnhgk tftctaaype sktpltatls ksgntfirpev hllpppseel
	241 alnelvtltc largfspkdv lvrwlqgsqe lprekyltwa srqepsqgtt tfavtsilrv
	301 aaedwkkgt fscmvgheal plaftqktid rlagkpthvn vsvvmaevdg tcy
GenBank 1F6A_B	
<i>Homo sapiens</i> IgE Fc (amino acids 6-222) (SEQ ID NO:210)	
212 aa	
	1 adpcdsnprg vsaylsrpsp fdlfirkst itclvvdlap skgtvnltws rasgkpvnhs
	61 trkeekqrng tltvtstlpv gtrdwieget yqcrvthphl pralmrsttk tsgraaapev
	121 yafatpewpg srdkrtlac1 ignfmpedis vqwlhnevql pdarhsttqp rktkgsghfv
	181 fsrlevtrae weqkdeficr avheaaspsq tvgravsvnp gk
GenBank P01861	
<i>Homo sapiens</i> IgG4 Fc (amino acids 100-327) (SEQ ID NO:211)	
228 aa	
	1 astkqpsvfp lapcsrste staaigclvk dyfpeptvs wnsгалtsgv htfpavlqss
	61 glyslssvt vpssslgtkt ytcnvdhkps nt kvdkrves kygppcpscp afe1ggpsv
	121 flfppkpkdt lmisrtpevt cvvvdvsqed pevqfnwyvd gvevhnaktk preeqfnsty
	181 rvsvlvtvlh qdwlngkeyk ckvsnkglps siektiskak gqprepqvyt lppsqeemtk
	241 nqvsltclvk gfypsdiave wesngqpenn ykttppvlds dgsfflysr1 tvdksrwqeg
	301 nvfscsvmhe alnhnytqks ls1slgk

FIG. 2D

WT Human IgG1 Fc Sequence: (SEQ ID NO:212)

DKTHTCPPCPAPELGGPSVFLFPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY~~STY~~
 RVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
 ESNQGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 2E

Human IgG1 Fc Mutant: L234F/L235E/P331S (Triple Mutant "TM") (SEQ ID NO:213)

DKTHTCPPCPAPEFEGGPSVFLFPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY~~STY~~
 RVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
 ESNQGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 2F

Human IgG1 Fc Mutant: N297A (SEQ ID NO:214)

DKTHTCPPCPAPELGGPSVFLFPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY~~STY~~
 RVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
 ESNQGPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 2G

Human IgG1 Fc Mutant: L234A/L235A ("LALA") (SEQ ID NO:215)

DKTHTCPPCPAPEAAGGPSVFLFPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY~~NST~~
 YRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE
 WESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Residue numbered according to EU index (Kabat Numbering)

Figure 3A
Homo sapiens
GenBank NP_001229687
HLA-A
Amino acids 25-365 (SEQ ID NO:216)

```
1  mavmaprtll  lllsgalalt  qtwagshsmr  yfftsvsrpg  rgeprfiavg  yvddtqfvrf
61  dsdaasqkme  prapwiegeg  peywdqetrn  mkahsqtdra  nlgtrgyyn  qsedgshtiq
121  imygcdvgrp  grflrgyrqd  aydgkdyial  nedlrswtaa  dmaaqitkrk  weavhaaeqr
181  rvylegrcvd  glrrylengk  etlgrtdppk  thmthhpisd  heatlrcwal  gfypaeitlt
241  wqrddgedtq  dtelvetrpa  gdgtfqkwa  vvvpssgeeq  ytchvqhegl  pkpltlrwl
301  ssqptipivg  iiaqlvllga  vitgavvaav  mwrrkssdrk  ggsytqaass  dsaggdsdvs
361  tackv
```

Figure 3B
Homo sapiens
GenBank NP_005505
HLA-B
Amino acids 25-362 (SEQ ID NO:217)

```
1  mlvmaprtvl  lllsaalalt  etwagshsmr  yfytsvsrpg  rgeprfivsg  yvddtqfvrf
61  dsdaaspre  prapwiegeg  peywdrntqi  ykaqaqtdre  slrnlrgyyn  qseagshtlq
121  smygcdvgrp  grllrghdqy  aydgkdyial  nedlrswtaa  dtaaqitqrk  weaareaeqr
181  raylegecve  wlrrylengk  dkleradppk  thvthhpisd  heatlrcwal  gfypaeitlt
241  wqrddgedtq  dtelvetrpa  gdrtfqkwa  vvvpssgeeq  ytchvqhegl  pkpltlrwl
301  ssqstvpi  ivaglavlav  vvigavvaav  mcrkssggk  ggsysqaacs  dsaggdsdvs
361  ta
```

Figure 3C*Homo sapiens*

GenBank NP_001229971

HLA-C

Amino acids 25-366 (SEQ ID NO:218)

```

1  mrvmaprall lllsgglalt etwacshsmr yfdtavsrpg rgeprfisvg yvddtqfvrfrf
61  dsdaasprge prapwveqeg peywdretqn Ykrqaqadirv slrnlrqyyyn qsedgshtlq
121 rmygcdlgpd grllrgyqds aydgkdyial nedlrswtaa dtaaqitqrk leaaraaeql
181 raylegtcve wlrrylengk etlqraepk thvthhplsd heatlrcwal gfypaeitlt
241 wqrddgedtq dtelvetrpa gdgtfqkwa vvpvsggeqr ytchmqhegl qepltlswep
301 ssqptiping ivaglavlvv lavlgavvta mmcrkssgg kggscsqaac snsaggdsdes
361 litcka

```

FIG. 4

NP_004039.1	msrvalavlallslsgleaiqrtpkqiqvysrhpaengksnflncyvsgfhpsdievdll	60
NP_001009066.1	msrvalavlallslsgleaiqrtpkqiqvysrhpaengksnflncyvsgfhpsdievdll	60
NP_001040602.1	msrvalavlallslsgleaiqrtpkqiqvysrhppengkpnflncyvsgfhpsdievdll	60
NP_776318.1	marfvalvllgllslsgldaiqrppkqiqvysrhppedgkpnynlncyvvygfhppqieidl	60
NP_033865.2	marsvtlvflvsltglyaiqktpqiqvysrhppengkpnlnlncyvtqfhpphieiqml	60
	:	
NP_004039.1	kngeriekvehsdlsfskdwsfyllyyteftptekdeyacrvnhvtlsqpkivkwdrdm	119 (SEQ ID NO:49)
NP_001009066.1	kngeriekvehsdlsfskdwsfyllyyteftptekdeyacrvnhvtlsqpkivkwdrdm	119 (SEQ ID NO:49)
NP_001040602.1	kngckmgkvehsdlsfskdwsfyllyyteftptnekdeyacrvnhvtlsqprtvkwdrdm	119 (SEQ ID NO:50)
NP_776318.1	kngckik-seqsdlsfskdwsfyllshaeftpnskdqyscrvkhvtleqpriwkwdrdl	118 (SEQ ID NO:51)
NP033865	kngkkipkvemsdmsfskdwsfyllahtefptetdttyacrvkhasmaepkvtvywdrdm	119 (SEQ ID NO:52)
	::: * **:::**:*:::*****...* **:::*****:*::: * * *****:	

FIG. 5A***HLA-A***

GSHSMRYFFTSVSRPGRGEPRIA VGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVK AHSQTHRVDLGTLRGYYNQSEAGSHTVQRMYGCDVGSD
WRFLRGYHQYAYDGKD YIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLR
AYLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFP
AEITLTWQRDGEDQTQDTEL VETRPAGDGT FQKWA AVVVPSGQE QRYTCHVQH
EGLPKPLTLRWEP (SEQ ID NO:53)

FIG. 5B***HLA-A (Y84A; A236C)***

GSHSMRYFFTSVSRPGRGEPRIA VGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVK AHSQTHRVDLGTLRG AYNQSEAGSHTVQRMYGCDVGSD
WRFLRGYHQYAYDGKD YIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQLR
AYLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFP
AEITLTWQRDGEDQTQDTEL VETRP CGDGT FQKWA AVVVPSGQE QRYTCHVQH
EGLPKPLTLRWEP (SEQ ID NO:225)

FIG. 5C***HLA-A (Y84C; A139C)***

GSHSMRYFFTSVSRPGRGEPRIA VGYVDDTQFVRFDSDAASQRMEPRAPWIEQE
GPEYWDGETRKVK AHSQTHRVDLGTLRG CYNQSEAGSHTVQRMYGCDVGSD
WRFLRGYHQYAYDGKD YIALKEDLRSWTAADM CAQTTKHKWEAAHVAEQLR
AYLEGTCVEWLRRYLENGKETLQRTDAPKTHMTHHAVSDHEATLRCWALSFP
AEITLTWQRDGEDQTQDTEL VETRPAGDGT FQKWA AVVVPSGQE QRYTCHVQH
EGLPKPLTLRWEP (SEQ ID NO:226)

FIG. 5D***HLA-A A11***

GSHSMRYFYTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRM EPRAPWIEQ
EGPEYWDQETRNVKAQSQTDRVDLGTLRGYYNQSEDGSHTIQIMYGCDVGP DG
RFLRGYRQDAYDGKD YIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAY
LEGTCVEWLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYP AEI
TLTWQRDGEDQTQDTEL VETRPAGDGT FQKWAAVVVPSGEEQRYTCHVQHEG
LPKPLTLRWE (SEQ ID NO:227)

FIG. 5E***HLA-A A11 (Y84A; A236C)***

GSHSMRYFYTSVSRPGRGEPRFIAVG YVDDTQFVRFDSDAASQRM EPRAPWIEQ
EGPEYWDQETRNVKAQSQTDRVDLGTLRG AYNQSEDGSHTIQIMYGCDVGP DG
RFLRGYRQDAYDGKD YIALNEDLRSWTAADMAAQITKRKWEAAHAAEQQRAY
LEGTCVEWLRRYLENGKETLQRTDPPKTHMTHHPISDHEATLRCWALGFYP AEI
TLTWQRDGEDQTQDTEL VETRP CGDGT FQKWAAVVVPSGEEQRYTCHVQHEG
LPKPLTLRWE (SEQ ID NO:228)

FIG. 5F***HLA-B***

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE
GPEYWDRNTQIYKAQAQTDRESLRNLRGYYNQSEAGSHTLQSMYGCDVGPDGR
LLRGHDQYAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLE
GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYPAEITL
TWQRDGEDQTQDTELVETRPAGDRTFQKWA~~AVVV~~PSGEEQRYTCHVQHEGLP
KPLTLRWEP (SEQ ID NO:229)

FIG. 5G***HLA-B (Y84A; A236C)***

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE
GPEYWDRNTQIYKAQAQTDRESLRNLRGAYNQSEAGSHTLQSMYGCDVGPDGR
LLRGHDQYAYDGKDYIALNEDLRSWTAADTAAQITQRKWEAAREAEQRRAYLE
GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYPAEITL
TWQRDGEDQTQDTELVETRPCGDRTFQKWA~~AVVV~~PSGEEQRYTCHVQHEGLP
KPLTLRWEP (SEQ ID NO:230)

FIG. 5H***HLA-B (Y84C; A139C)***

GSHSMRYFYTSVSRPGRGEPRFISVGYVDDTQFVRFDSDAASPREEPRAPWIEQE
GPEYWDRNTQIYKAQAQTDRESLRNLRGCYNQSEAGSHTLQSMYGCDVGPDGR
LLRGHDQYAYDGKDYIALNEDLRSWTAADTCAQITQRKWEAAREAEQRRAYLE
GECVEWLRRYLENGKDKLERADPPKTHVTHHPISDHEATLRCWALGFYPAEITL
TWQRDGEDQTQDTELVETRPAGDRTFQKWA~~AVVV~~PSGEEQRYTCHVQHEGLP
KPLTLRWEP (SEQ ID NO:231)

FIG. 5I***HLA-C***

CSHSMRYFDTAVSRPGRGEPFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ
EGPEYWDRETQNYKRQAQADRVSLRNLRGYYNQSEDGSHTLQRMYGCDLGPD
GRLLRGYDQSAYDGKDYIALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAY
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEI
TLTWQRDGEDQTQDTEL VETRPAGDGTQKWA AVVVPSGQEQRYTCHMQHEG
LQEPLTSLWEP (SEQ ID NO:232)

FIG. 5J***HLA-C (Y84A; A236C)***

CSHSMRYFDTAVSRPGRGEPFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ
EGPEYWDRETQNYKRQAQADRVSLRNLRGA^AYNQSEDGSHTLQRMYGCDLGPD
GRLLRGYDQSAYDGKDYIALNEDLRSWTAADTAAQITQRKLEAARAAEQLRAY
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEI
TLTWQRDGEDQTQDTEL VETRPC^GGDGTQKWA AVVVPSGQEQRYTCHMQHEG
LQEPLTSLWEP (SEQ ID NO:233)

FIG. 5K***HLA-C (Y84C; A139C)***

CSHSMRYFDTAVSRPGRGEPFISVGYVDDTQFVRFDSDAASPRGEPRAPWVEQ
EGPEYWDRETQNYKRQAQADRVSLRNLRG^CYNQSEDGSHTLQRMYGCDLGPD
GRLLRGYDQSAYDGKDYIALNEDLRSWTAADT^CAQITQRKLEAARAAEQLRAY
LEGTCVEWLRRYLENGKETLQRAEPPKTHVTHHPLSDHEATLRCWALGFYPAEI
TLTWQRDGEDQTQDTEL VETRPAGDGTQKWA AVVVPSGQEQRYTCHMQHEG
LQEPLTSLWEP (SEQ ID NO:234)

FIG. 6A

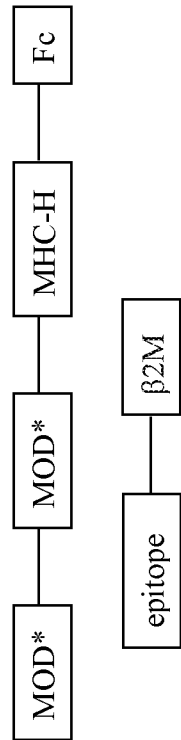


FIG. 6B

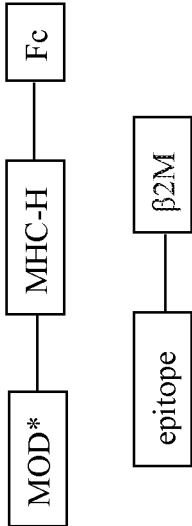


FIG. 6C

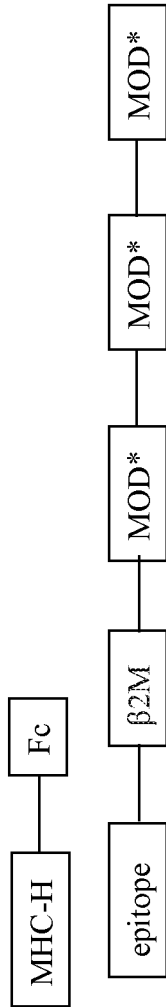


FIG. 6D

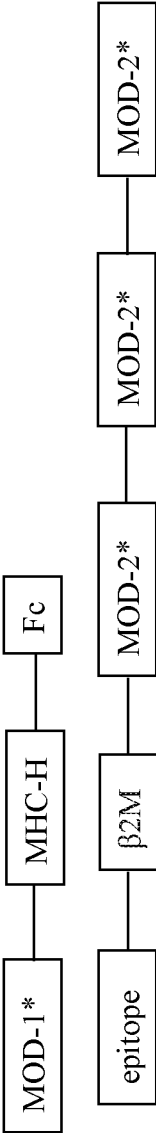


FIG. 7A

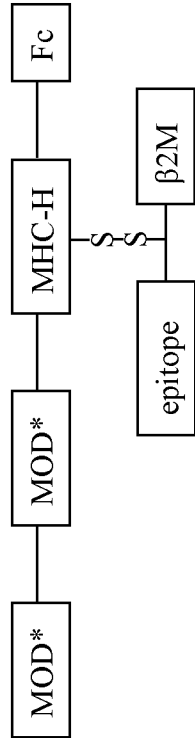


FIG. 7B

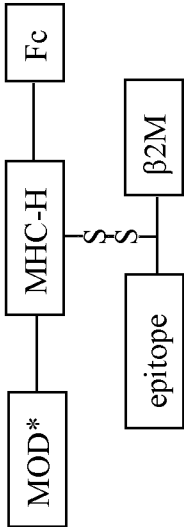


FIG. 7C

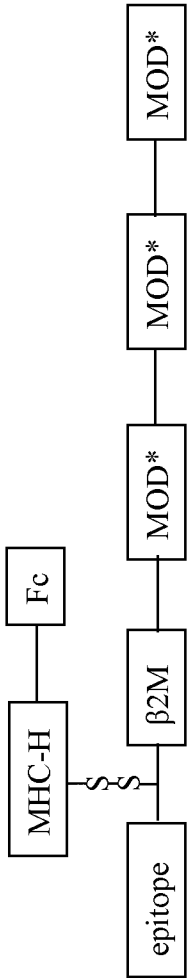


FIG. 7D

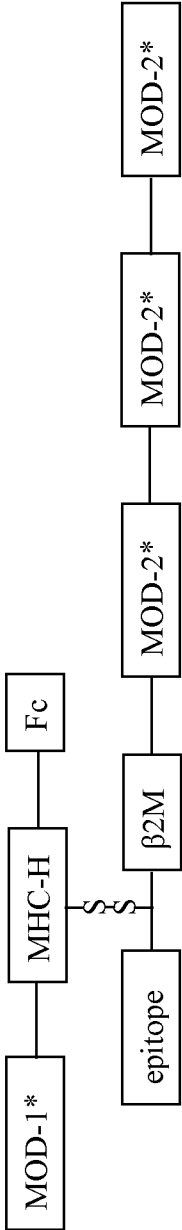


Fig. 8

HLA-A	GSHSMRYFFTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQKMEPRAPWIEQEGPEYW
HLA-B	GSHSMRYFYTSVSRPGRGEPRI SVGYVDDTQFVRFDSDAASPREEPAPWIEQEGPEYW
HLA-C	CSHSMRYFDTAVSRPGRGEPRI SVGYVDDTQFVRFDSDAASPRGEPAPWIEQEGPEYW
HLA-A*0201	GSHSMRYFFTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
Mouse H2K	GPHSLRYFVTAVSRPGLGEPRIAVGYVDDTQFVRFDSDADNPRFEPAPWMEQEGPEYW
HLA_A(var. 2)	GSHSMRYFFTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
HLA_A(var. 2C)	GSHSMRYFFTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
HLA-A(var.2CP)	GSHSMRYFFTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
HLA-A*1101	GSHSMRYFYTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
HLA-A*2402	GSHSMRYFSTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW
HLA-A*3303	GSHSMRYFTTSVSRPGRGEPRIAVGYVDDTQFVRFDSDAASQRMPEPRAPWIEQEGPEYW

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84

HLA-A	DQETRNMKAHSQTDRLNLTGLRGYNQSEAGSHTIQIMYGCDVGPDRFLRGYRQDAYDG
HLA-B	DRNTQIYKAAQTDRESLRNLRGYNQSEAGSHTLQSMYGCDVGPDRLLRGHDQYAYDG
HLA-C	DRETQNYKRQAQADRVSLRNLRGYNQSEAGSHTLQRMYGCDLGPDRLLRGYDQSAAYDG
HLA-A*0201	DGETRKVKAHSQTHRVDLGTGLRGYNQSEAGSHTVQRMYGCDVGS DWRFLRGYHQYAYDG
MOUSE H2K	EEQTQRAKSDEQWFRVSLRTAQRYYNQSKGGSHTFQRMFGCDVGS DWRLLRGYQQFAYDG
HLA_A(var. 2)	DGETRKVKAHSQTHRVDLGTGLRGYNQSEAGSHTVQRMYGCDVGS DWRFLRGYHQYAYDG
HLA_A(var. 2C)	DGETRKVKAHSQTHRVDLGTGLRGYNQSEAGSHTVQRMYGCDVGS DWRFLRGYHQYAYDG
HLA-A(var.2CP)	DGETRKVKAHSQTHRVDLGTGLRGYNQSEAGSHTVQRMYGCDVGS DWRFLRGYHQYAYDG
HLA-A*1101	DQETRN VKAQSQTDRVDLGTGLRGYNQSEAGSHTIQIMYGCDVGPDRFLRGYRQDAYDG
HLA-A*2402	DEETGKVKAHSQTDRENLR LIALRYYNQSEAGSHTLQMMFGCDVGS DGRFLRGYHQYAYDG
HLA-A*3303	DRNTRNVKAHSQIDRVDLGTGLRGYNQSEAGSHTIQMMYGCDVGS DGRFLRGYQQDAYDG

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139

HLA-A	KDYIALNEDLRSWTAADMAAQITKRRKWEAVHAAEQRRVYLEGRCVDGLRRYLENGKETLQ
HLA-B	KDYIALNEDLRSWTAADTAAQITQRRKWEAAREAEQRRAYLEGECEVWLRRYLENGKDKLE
HLA-C	KDYIALNEDLRSWTAADTAAQITQRRKLEAARAAEQRLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A*0201	KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQRLRAYLEGTCVEWLRRYLENGKETLQ
MOUSE H2K	RDYIALNEDLKTWTAADTAALITRRKWEQAGDAEYRAYLEGECEVWLRRYLELGNETLL
HLA_A(var. 2)	KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQRLRAYLEGTCVEWLRRYLENGKETLQ
HLA_A(var. 2C)	KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQRLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A(var.2CP)	KDYIALKEDLRSWTAADMAAQTTKHKWEAAHVAEQRLRAYLEGTCVEWLRRYLENGKETLQ
HLA-A*1101	KDYIALNEDLRSWTAADMAAQITKRRKWEAAHAAEQRRAYLEGRCVEWLRRYLENGKETLQ
HLA-A*2402	KDYIALKEDLRSWTAADMAAQITKRRKWEAAHVAEQRRAYLEGTCDVGLRRYLENGKETLQ
HLA-A*3303	KDYIALNEDLRSWTAADMAAQITQRRKWEAARVAEQRLRAYLEGTCVEWLRRYLENGKETLQ

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236

aac5	aac6
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HLA-A	QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:242)
HLA-B	QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:243)
HLA-C	QKWAAVVVPSGQEQRYTCHMQHEGLQEPLTLSWE	(SEQ ID NO:244)
HLA-A*0201	QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:53)
MOUSE H2K	QKWAAVVVPLGKEQNYTCHVHHKGLPEPLTLRW	(SEQ ID NO:54)
HLA_A (var. 2)	QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:245)
HLA_A (var. 2C)	QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:246)
HLA-A (var. 2CP)	QKWAAVVVPSGQEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:247)
HLA-A*1101	QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWEL	(SEQ ID NO:248)
HLA-A*2402	QKWAAVVVPSGEEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:249)
HLA-A*3303	QKWASVVVPSGQEQRYTCHVQHEGLPKPLTLRWE	(SEQ ID NO:250)
	*****:***** *:***:*****::*****:***** *	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/049756

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/00; A61K 39/395; C07K 14/725; C07K 14/73; C07K 14/735 (2018.01)

CPC - A61K 39/00; A61K 39/39; C07K 14/70539; C07K 2317/52; C07K 2319/30; C07K 2319/40 (2018.08)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 424/193.1; 435/334; 435/343; 435/372; 435/375; 435/372.3; 530/350 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2017/0058015 A1 (ALBERT EINSTEIN COLLEGE OF MEDICINE) 02 March 2017	1, 2, 13, 14, 20, 21
--	(02.03.2017) entire document	-----
Y		3
Y	ARDUIN et al. "Highly reduced binding to high and low affinity mouse Fc gamma receptors by L234A/L235A and N297A Fc mutations engineered into mouse IgG2a," Molecular Immunology, 18 October 2014 (18.10.2014), Vol. 63, No. 2, Pgs. 456-463. entire document	3
A	WO 2015/195531 A2 (ALBERT EINSTEIN COLLEGE OF MEDICINE, INC.) 23 December 2015 (23.12.2015) entire document	1-3, 13, 14, 20, 21
A	WO 2015/112541 A2 (ALBERT EINSTEIN COLLEGE OF MEDICINE) 30 July 2015 (30.07.2015) entire document	1-3, 13, 14, 20, 21
A	WO 2002/087613 A1 (OREGON HEALTH AND SCIENCE UNIVERSITY) 07 November 2002 (07.11.2002) entire document	1-3, 13, 14, 20, 21

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

17 October 2018

Date of mailing of the international search report

19 NOV 2018

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, VA 22313-1450
Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/049756

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 4-12, 15-19
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

CUEB-110W0_SEQUENCE_LISTING_ST25.txt
SEQUENCE LISTING

<110> Seidel, Ronald D III
Chaparro, Rodolfo J

<120> Multimeric T-Cell Modulatory Polypeptides and Methods of Use
Thereof

<130> CUEB-110W0

<150> US62/555,499
<151> 2017-09-07

<160> 251

<170> PatentIn version 3.5

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<213> Homo sapiens

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Gly	Ser	Asn	Met	Thr	Ile	Glu	Cys	Lys	Phe	Pro	Val	Glu	Lys	Gln	Leu
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Ile	Gln	Phe	Val	His	Gly	Glu	Glu	Asp	Leu	Lys	Val	Gln	His	Ser	Ser
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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
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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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115 120 125

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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
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20 25 30

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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

35

40

45

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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
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Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
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<213> Homo sapiens

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35 40 45

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50 55 60

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65 70 75 80

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro Cys Val Pro Glu
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Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly Met Gly Thr Ser
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260 265

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20 25 30

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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

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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

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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
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Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
210 215 220

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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40

45

Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly Gly
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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
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100 105 110

Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
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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

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

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210 215 220

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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
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100 105 110

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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
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Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
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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

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100 105 110

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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115 120 125

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165 170

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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115 120 125

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Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

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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
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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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Cys Arg Gln Cys Lys Gly Val Phe Arg Thr Arg Lys Glu Cys Ser Ser
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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

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20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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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
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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
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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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100 105 110

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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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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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

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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 133
<212> PRT
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<220>
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<220>
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<222> (42)..(42)
<223> any amino acid other than phenylalanine

<400> 19

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>  20
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<212>  PRT
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<220>
<223>  Synthetic polypeptide

<220>
<221>  Misc_feature
<222>  (20)..(20)
<223>  any amino acid other than aspartic acid

<400>  20

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

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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

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<210> 21
<211> 133
<212> PRT
<213> Artificial sequence
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<220>
<223> Synthetic polypeptide

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<220>
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<222> (15)..(15)
<223> any amino acid other than glutamic acid
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<400> 21

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

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<210> 22
<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
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<400> 22

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

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<210> 23
<211> 133
<212> PRT
<213> Artificial sequence
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<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feature
<222> (45)..(45)
<223> any amino acid other than tyrosine
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<400> 23

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>	24
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<212>	PRT
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<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feature
<222> (126)..(126)
<223> any amino acid other than glutamine
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<400> 24

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>	25
<211>	133
<212>	PRT
<213>	Artificial sequence

<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feature
<222> (16)..(16)
<223> any amino acid other than histidine
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<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than phenylalanine
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<400> 25

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 26
<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

<400> 26

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 27
 <211> 133
 <212> PRT
 <213> Artificial sequence

<220>
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<220>
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 <222> (15)..(15)
 <223> any amino acid other than glutamic acid

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 27

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> 28

<211> 133

<212> PRT

<213> Artificial sequence

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<221> Misc_feature

<222> (16)..(16)

<223> any amino acid other than histidine

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

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<223> any amino acid other than aspartic acid

<220>

<221> Misc_feature

<222> (42)..(42)

<223> any amino acid other than phenylalanine

<400> 28

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 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> 29

<211> 133

<212> PRT

<213> Artificial sequence

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<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> (126)..(126)

<223> any amino acid other than glutamine

<400> 29

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> 30
<211> 133
<212> PRT
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<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> 30

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 31
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<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> 31

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Xaa
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 32
<211> 133
<212> PRT
<213> Artificial sequence

<220>
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<220>
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<223> any amino acid other than aspartic acid

<220>
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<222> (42)..(42)
<223> any amino acid other than phenylalanine

<220>

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<221> Misc_feature
 <222> (45)..(45)
 <223> any amino acid other than tyrosine

<220>
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 <222> (126)..(126)
 <223> any amino acid other than glutamine

<400> 32

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> 33
 <211> 133
 <212> PRT
 <213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<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> 33

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
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 34
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<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> 34

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 35
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 35

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
1 5

<210> 36
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 36

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 37
 <211> 10
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 37

Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu
1				5					10

<210> 38
 <211> 5
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 38

His	His	His	His	His
1				5

<210> 39
 <211> 6
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 39

His	His	His	His	His	His
1					5

<210> 40
 <211> 8
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 40

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Trp Ser His Pro Gln Phe Glu Lys
1 5

<210> 41
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 41

Arg Tyr Ile Arg Ser
1 5

<210> 42
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 42

Phe His His Thr
1

<210> 43
<211> 17
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 43

Trp Glu Ala Ala Ala Arg Glu Ala Cys Cys Arg Glu Cys Cys Ala Arg
1 5 10 15

Ala

<210> 44

<211> 8
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 44

Leu Glu Val Leu Phe Gln Gly Pro
 1 5

<210> 45
 <211> 7
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 45

Glu Asn Leu Tyr Thr Gln Ser
 1 5

<210> 46
 <211> 5
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 46

Asp Asp Asp Asp Lys
 1 5

<210> 47
 <211> 4
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 47

Leu Val Pro Arg

1

<210> 48
 <211> 22
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

 <400> 48

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> 49
 <211> 119
 <212> PRT
 <213> Homo sapiens

 <400> 49

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 50
 <211> 119
 <212> PRT
 <213> Macaca mulatta

<400> 50

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> 51
 <211> 118
 <212> PRT
 <213> Bos Taurus

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 51

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> 52

<211> 119

<212> PRT

<213> Mus musculus

<400> 52

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 53
<211> 276
<212> PRT
<213> Homo sapiens

<400> 53

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 54
 <211> 274
 <212> PRT
 <213> Mus musculus

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 54

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 55
<211> 99
<212> PRT
<213> Homo sapiens

<400> 55

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Arg Asp Met

<210> 56
 <211> 99
 <212> PRT
 <213> Homo sapiens

<400> 56

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> 57
 <211> 276
 <212> PRT
 <213> Homo sapiens

<400> 57

Gly	Ser	His	Ser	Met	Arg	Tyr	Phe	Phe	Thr	Ser	Val	Ser	Arg	Pro	Gly
1				5					10					15	

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 58
<211> 275
<212> PRT
<213> Homo sapiens

<400> 58

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 59

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (4)..(4)
 <223> Xaa is any amino acid other than proline

<400> 59

Val Pro Gly Xaa Gly
 1 5

<210> 60
 <211> 5
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 60

Gly Ser Gly Gly Ser
 1 5

<210> 61
 <211> 4
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 61

Gly Gly Gly Ser
 1

<210> 62
 <211> 4
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<400> 62

Gly Gly Ser Gly
 1

<210> 63
 <211> 5
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

 <400> 63

 Gly Gly Ser Gly Gly
 1 5

<210> 64
 <211> 5
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

 <400> 64

 Gly Ser Gly Ser Gly
 1 5

<210> 65
 <211> 5
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

 <400> 65

 Gly Ser Gly Gly Gly
 1 5

<210> 66
 <211> 5
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

 <400> 66

Gly Gly Gly Ser Gly
1 5

<210> 67
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 67

Gly Ser Ser Ser Gly
1 5

<210> 68
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (1)..(5)
<223> This stretch of residues may be repeated

<400> 68

Gly Ser Ser Ser Ser
1 5

<210> 69
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (1)..(5)
<223> This stretch of residues may be repeated

<400> 69

Gly Gly Gly Gly Ser
1 5

<210> 70

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 70

Ala Ala Ala Gly Gly
1 5

<210> 71

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 71

Gly Cys Gly Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 72

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 72

Leu Leu Met Gly Thr Leu Gly Ile Val
1 5

<210> 73

<211> 8

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 73

Thr Leu Gly Ile Val Cys Pro Ile
1 5

<210> 74

<211> 10

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 74

Tyr Met Leu Asp Leu Gln Pro Glu Thr Thr
1 5 10

<210> 75

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<400> 75

Tyr Met Leu Asp Leu Gln Pro Glu Thr
1 5

<210> 76

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (8)..(8)

<223> any amino acid other than aspartic acid

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 76

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> 77

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (36)..(36)

<223> any amino acid other than isoleucine

<400> 77

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 78
<211> 219
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (54)..(54)
<223> any amino acid other than glutamic acid

<400> 78

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 79

<211> 208

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (19)..(19)

<223> any amino acid other than asparagine

<400> 79

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
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 80
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (63)..(63)
<223> any amino acid other than asparagine

<400> 80

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 81
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (67)..(67)
<223> any amino acid other than isoleucine

<400> 81

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 82

<211> 208

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (86)..(86)

<223> any amino acid other than lysine

<400> 82

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
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

180

185

190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 83

<211> 208

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (157)..(157)

<223> any amino acid other than glutamine

<400> 83

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 84

<211> 208

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (158)..(158)

<223> any amino acid other than aspartic acid

<400> 84

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 85

<211> 208

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (25)..(25)

<223> any amino acid other than leucine

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 85

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> 86
 <211> 208
 <212> PRT
 <213> Artificial sequence

 <220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (31)..(31)
 <223> any amino acid other than tyrosine

<400> 86

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 87
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (33)..(33)
<223> any amino acid other than glutamine

<400> 87

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>	88
<211>	208
<212>	PRT
<213>	Artificial sequence

<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feautre
<222> (38)..(38)
<223> any amino acid other than methionine
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<400> 88

Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu Ser Cys

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

1	5	10	15
Gly	His	Asn	Val
	20		
Ser	Val	Glu	Glu
		25	
Leu	Ala	Gln	Thr
			30
Arg	Ile	Tyr	Trp
Gln	Lys	Glu	Lys
	35		
Lys	Lys	Xaa	Val
		40	
Leu	Thr	Met	Met
			45
Ser	Gly	Asp	Met
			Asn
Ile	Trp	Pro	Glu
	50		
Tyr	Lys	Asn	Arg
		55	
Thr	Ile	Phe	Asp
			60
Ile	Thr	Asn	Asn
Leu	Ser	Ile	Val
	65		
Ile	Leu	Ala	Leu
		70	
Arg	Pro	Ser	Asp
		75	
Glu	Gly	Thr	Tyr
			80
Glu	Cys	Val	Val
		85	
Leu	Lys	Tyr	Glu
			90
Lys	Asp	Ala	Phe
			95
Lys	Arg	Glu	His
Leu	Ala	Glu	Val
		100	
Thr	Leu	Ser	Val
			105
Lys	Ala	Asp	Phe
			110
Pro	Thr	Pro	Ser
Ile	Ser	Asp	Phe
	115		
Glu	Ile	Pro	Thr
			120
Ser	Asn	Ile	Arg
			125
Arg	Ile	Ile	Cys
Ser	Thr	Ser	Gly
	130		
Gly	Gly	Phe	Pro
			135
Glu	Pro	His	Leu
			140
Ser	Trp	Leu	Glu
			Asn
Gly	Glu	Glu	Leu
	145		
Asn	Ala	Ile	Asn
			150
Thr	Thr	Val	Ser
			155
Gln	Asp	Pro	Glu
			160
Thr	Glu	Leu	Tyr
		165	
Ala	Val	Ser	Ser
			170
Lys	Leu	Asp	Phe
			175
Asn	Met	Thr	Thr
Asn	His	Ser	Phe
		180	
Met	Cys	Leu	Ile
			185
Lys	Tyr	Gly	His
			190
Leu	Arg	Val	Asn
Gln	Thr	Phe	Asn
	195		
Trp	Asn	Thr	Thr
			200
Lys	Gln	Glu	His
			205
Phe	Pro	Asp	Asn

<210> 89

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<211> 208
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (39)..(39)
 <223> any amino acid other than valine

<400> 89

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
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 90
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (49)..(49)
<223> any amino acid other than isoleucine

<400> 90

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 91
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (53)..(53)
<223> any amino acid other than tyrosine

<400> 91

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 92

<211> 208

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (60)..(60)

<223> any amino acid other than aspartic acid

<400> 92

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 93
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (108)..(108)
<223> any amino acid other than phenylalanine

<400> 93

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 94
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (156)..(156)
<223> any amino acid other than serine

<400> 94

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 95

<211> 208

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (111)..(111)

<223> any amino acid other than proline

<400> 95

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

180

185

190

Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro Asp Asn
195 200 205

<210> 96

<211> 224

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (61)..(61)

<223> any amino acid other than asparagine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 97
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (66)..(66)
<223> any amino acid other than aspartic acid

<400> 97

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 98

<211> 224

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (70)..(70)

<223> any amino acid other than tryptophan

<400> 98

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 99
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (91)..(91)
<223> any amino acid other than histidine

<400> 99

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 100
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<400> 100

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

1	5	10	15
Cys	Gln	Phe	Ala
	20	Asn	Ser
Gln	Asn	Gln	Ser
	25	Leu	Ser
Glu	Leu	Val	Val
	30		
Phe	Trp	Gln	Asp
	35	Gln	Glu
Asn	Leu	Val	Leu
	40	Asn	Glu
Val	Tyr	Leu	Gly
	45		
Lys	Glu	Lys	Phe
	50	Asp	Ser
Val	His	Ser	Lys
	55	Tyr	Met
Xaa	Arg	Thr	Ser
	60		
Phe	Asp	Ser	Asp
	65	Ser	Trp
Thr	Leu	Arg	Leu
	70	His	Asn
Leu	Gln	Ile	Lys
	75		80
Asp	Lys	Gly	Leu
	85	Tyr	Gln
Cys	Ile	Ile	His
	90	His	Lys
Lys	Lys	Pro	Thr
	95	Gly	
Met	Ile	Arg	Ile
	100	His	Gln
Met	Asn	Ser	Glu
	105	Leu	Ser
Val	Leu		
	110		

<210> 101
 <211> 110
 <212> PRT
 <213> Artificial sequence
 <220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (66)..(66)
 <223> any amino acid other than aspartic acid

<400> 101

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 102
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (70)..(70)
<223> any amino acid other than tryptophan

<400> 102

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

```

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>  103
<211>  110
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic polypeptide

<220>
<221>  Misc_feature
<222>  (91)..(91)
<223>  any amino acid other than histidine

<400>  103

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

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CUEB-110WO_SEQUENCE_LISTING_ST25.txt

100

105

110

<210> 104
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (41)..(41)
<223> any amino acid other than valine

<400> 104

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 105
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (41)..(41)
<223> any amino acid other than valine

<400> 105

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 106
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (35)..(35)
<223> any amino acid other than glutamine

<400> 106

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 107
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (35)..(35)
<223> any amino acid other than glutamine

<400> 107

Ala Pro Leu Lys Ile Gln Ala Tyr Phe Asn Glu Thr Ala Asp Leu Pro

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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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

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<210> 108
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feature
<222> (33)..(33)
<223> any amino acid other than phenylalanine

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```

<400> 108

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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

```

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 109
<211> 110
<212> PRT
<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (33)..(33)

<223> any amino acid other than phenylalanine

<400> 109

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> 110

<211> 224

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (72)..(72)

<223> any amino acid other than leucine

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 110

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

195

200

205

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
210 215 220

<210> 111
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (72)..(72)
<223> any amino acid other than leucine

<400> 111

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> 112

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<211> 224
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (59)..(59)
 <223> any amino acid other than tyrosine

<400> 112

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 113
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (59)..(59)
<223> any amino acid other than tyrosine

<400> 113

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>	114
<211>	224
<212>	PRT
<213>	Artificial sequence

<220>
<223> Synthetic polypeptide

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<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine
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<220>
<221>  Misc_feature
<222>  (91)..(91)
<223>  any amino acid other than histidine
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<400> 114

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 115
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

<220>
<221> Misc_feature

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<222> (91)..(91)

<223> any amino acid other than histidine

<400> 115

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> 116

<211> 224

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 116

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile Pro
 210 215 220

<210> 117
 <211> 110
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (17)..(17)
 <223> any amino acid other than asparagine

<220>
 <221> misc_feature
 <222> (66)..(66)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> Misc_feature
 <222> (91)..(91)
 <223> any amino acid other than histidine

<400> 117

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 118
<211> 224
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<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> 118

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 119
<211> 110
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (61)..(61)
<223> any amino acid other than asparagine

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<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> 119

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> 120

<211> 174

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (47)..(47)

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<223> any amino acid other than lysine

<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 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> 121

<211> 174

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (147)..(147)

<223> any amino acid other than glutamine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (11)..(11)
<223> any amino acid other than methionine

<400> 122

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (12)..(12)
<223> any amino acid other than phenylalanine

<400> 123

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (14)..(14)
<223> any amino acid other than glutamine

<400> 124

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (15)..(15)
<223> any amino acid other than leucine

<400> 125

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 126
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (16)..(16)
<223> any amino acid other than valine

<400> 126

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 127
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (18)..(18)

<223> any amino acid other than glutamine

<400> 127

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 128
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (19)..(19)
 <223> any amino acid other than asparagine

<400> 128

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (20)..(20)
<223> any amino acid other than valine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (21)..(21)
<223> any amino acid other than leucine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (22)..(22)
<223> any amino acid other than leucine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (23)..(23)
<223> any amino acid other than isoleucine

<400> 132

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 133
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (24)..(24)

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<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 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> 134

<211> 174

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (25)..(25)

<223> any amino acid other than glycine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (26)..(26)
<223> any amino acid other than proline

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (27)..(27)
<223> any amino acid other than leucine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (28)..(28)
<223> any amino acid other than serine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (29)..(29)
<223> any amino acid other than tryptophan

<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 Xaa Tyr Ser Asp
20 25 30

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 139
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (30)..(30)
<223> any amino acid other than tyrosine

<400> 139

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 140
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (31)..(31)

<223> any amino acid other than serine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 141
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (32)..(32)
 <223> any amino acid other than aspartic 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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (33)..(33)
<223> any amino acid other than proline

<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

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (34)..(34)
<223> any amino acid other than glycine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (35)..(35)
<223> any amino acid other than leucine

<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 Xaa Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
35 40 45

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 145
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (37)..(37)
<223> any amino acid other than glycine

<400> 145

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 146
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (38)..(38)

<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 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> 147

<211> 174

<212> PRT

<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (39)..(39)

<223> any amino acid other than serine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (40)..(40)
<223> any amino acid other than leucine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (41)..(41)
<223> any amino acid other than threonine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (42)..(42)
<223> any amino acid other than glycine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 151
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (43)..(43)
<223> any amino acid other than glycine

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 152
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (44)..(44)
<223> any amino acid other than leucine

<400> 152

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 153
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (45)..(45)

<223> any amino acid other than serine

<400> 153

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 154
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (46)..(46)
 <223> any amino acid other than tyrosine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> misc_feature
<222> (48)..(48)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> Misc_feature
<222> (52)..(52)
<223> any amino acid other than glutamic acid

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 156
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (49)..(49)
<223> any amino acid other than aspartic 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

Xaa Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
50 55 60

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 157
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (50)..(50)
<223> any amino acid other than threonine

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 158
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (51)..(51)
<223> any amino acid other than lysine

<400> 158

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 159
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (52)..(52)

<223> any amino acid other than glutamic acid

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 160
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (64)..(64)
 <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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (65)..(65)
<223> any amino acid other than phenylalanine

<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

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 162
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (66)..(66)
<223> any amino acid other than glutamine

<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 Xaa Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
65 70 75 80

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 163
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (67)..(67)
<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 164
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (68)..(68)
<223> any amino acid other than glutamic acid

<400> 164

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 165
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<222> (69)..(69)

<223> any amino acid other than leucine

<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 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> 166

<211> 174

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (70)..(70)

<223> any amino acid other than arginine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (71)..(71)
<223> any amino acid other than arginine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 168
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (72)..(72)
<223> any amino acid other than valine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 169
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (73)..(73)
<223> any amino acid other than valine

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 170
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (75)..(75)
<223> any amino acid other than glycine

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 171
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (76)..(76)
<223> any amino acid other than glutamic acid

<400> 171

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 172
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (77)..(77)

<223> any amino acid other than glycine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 173
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (78)..(78)
 <223> any amino acid other than serine

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (104)..(104)
<223> any amino acid other than aspartic acid

<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 Xaa Leu Pro Pro Ala Ser Ser Glu Ala
100 105 110

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 175
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (105)..(105)
<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

<210> 176
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (106)..(106)
<223> any amino acid other than proline

<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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 177
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (109)..(109)
<223> any amino acid other than serine

<400> 177

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 178
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<222> (110)..(110)

<223> any amino acid other than serine

<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 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> 179

<211> 174

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (111)..(111)

<223> any amino acid other than glutamic acid

<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 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 polypeptide

<220>
<221> Misc_feature
<222> (113)..(113)
<223> any amino acid other than arginine

<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

Xaa Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
115 120 125

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 181
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (114)..(114)
<223> any amino acid other than asparagine

<400> 181

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 182
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (115)..(115)
<223> any amino acid other than serine

<400> 182

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 183
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (117)..(117)
<223> any amino acid other than phenylalanine

<400> 183

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 184
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (130)..(130)
<223> any amino acid other than glutamine

<400> 184

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 185
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (131)..(131)

<223> any amino acid other than arginine

<400> 185

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 186
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (132)..(132)
 <223> any amino acid other than leucine

<400> 186

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 187
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (133)..(133)
<223> any amino acid other than glycine

<400> 187

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 188
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (134)..(134)
<223> any amino acid other than valine

<400> 188

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 189
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (135)..(135)
<223> any amino acid other than histidine

<400> 189

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 190
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (136)..(136)
<223> any amino acid other than leucine

<400> 190

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 191
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<222> (137)..(137)

<223> any amino acid other than histidine

<400> 191

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> 192

<211> 174

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic polypeptide

<220>

<221> Misc_feature

<222> (138)..(138)

<223> any amino acid other than threonine

<400> 192

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
165 170

<210> 193
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (139)..(139)
<223> any amino acid other than glutamic acid

<400> 193

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 194
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (141)..(141)
<223> any amino acid other than arginine

<400> 194

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 195
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (143)..(143)
<223> any amino acid other than arginine

<400> 195

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 196
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (144)..(144)
<223> any amino acid other than histidine

<400> 196

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 197
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (146)..(146)
<223> any amino acid other than tryptophan

<400> 197

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 198
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<221> Misc_feature

<222> (148)..(148)

<223> any amino acid other than leucine

<400> 198

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 199
 <211> 174
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic polypeptide

<220>
 <221> Misc_feature
 <222> (149)..(149)
 <223> any amino acid other than threonine

<400> 199

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 200
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (150)..(150)
<223> any amino acid other than glutamine

<400> 200

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 201
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (151)..(151)
<223> any amino acid other than glycine

<400> 201

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 202
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (153)..(153)
<223> any amino acid other than threonine

<400> 202

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 203
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<220>
<221> Misc_feature
<222> (154)..(154)
<223> any amino acid other than valine

<400> 203

Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 204
<211> 227
<212> PRT
<213> Homo sapiens

<400> 204

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Pro Gly Lys
225

<210> 205
<211> 325
<212> PRT
<213> Homo sapiens

<400> 205

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 206
<211> 246
<212> PRT
<213> Homo sapiens

<400> 206

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Leu Lys Thr
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 207
<211> 383
<212> PRT
<213> Homo sapiens

<400> 207

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 208
<211> 276
<212> PRT
<213> Homo sapiens

<400> 208

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 209
<211> 353
<212> PRT
<213> Homo sapiens

<400> 209

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 210
<211> 222
<212> PRT
<213> Homo sapiens

<400> 210

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 211
<211> 327
<212> PRT
<213> Homo sapiens

<400> 211

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 212
<211> 227
<212> PRT
<213> Homo sapiens

<400> 212

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 213
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<400> 213

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 214
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 214

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 215
<211> 227
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic polypeptide

<400> 215

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
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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 216
<211> 365
<212> PRT
<213> Homo sapiens

<400> 216

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 217
<211> 362
<212> PRT
<213> Homo sapiens

<400> 217

Met Leu Val Met Ala Pro Arg Thr Val Leu Leu Leu Leu Ser Ala Ala
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 218
<211> 366
<212> PRT
<213> Homo sapiens

<400> 218

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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 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
325 330 335

Ser Ser Gly Gly Lys Gly Gly Ser Cys Ser Gln Ala Ala Cys Ser Asn
340 345 350

Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Thr Cys Lys Ala
355 360 365

<210> 219
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 219

Gly Thr Leu Arg Gly
1 5

<210> 220
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 220

Tyr Asn Gln Ser Glu
1 5

<210> 221

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 221

Thr Ala Ala Asp Met
1 5

<210> 222

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 222

Ala Gln Thr Thr Lys
1 5

<210> 223

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 223

Val Glu Thr Arg Pro
1 5

<210> 224

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 224

Gly Asp Gly Thr Phe
1 5

<210> 225

<211> 276

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 225

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 226
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 226

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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
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
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			

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 227
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 227

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 228

<211> 275

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic sequence

<400> 228

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 229
<211> 276
<212> PRT
<213> Homo sapiens

<400> 229

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<210> 230
 <211> 276
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic sequence

<400> 230

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 231
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 231

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 232
<211> 276
<212> PRT
<213> Homo sapiens

<400> 232

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 233
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 233

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 234
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 234

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 235
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<220>
 <221> Misc_features
 <222> (6)..(10)
 <223> This stretch of residues may be repeated

<400> 235

Gly	Cys	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
1				5					10

<210> 236
 <211> 20
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic sequence

<400> 236

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> 237
 <211> 15
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic sequence

<400> 237

Gly	Cys	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser
1				5					10					15

<210> 238
 <211> 276
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Synthetic sequence

<220>
 <221> misc_feature
 <222> (79)..(83)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> (85)..(89)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> (134)..(138)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> (140)..(144)
 <223> Xaa can be any naturally occurring amino acid

<400> 238

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	Xaa	Xaa
65					70					75				80	

Xaa	Xaa	Xaa	Cys	Xaa	Xaa	Xaa	Xaa	Xaa	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		

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Tyr His Gln Tyr Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu
115 120 125

Asp Leu Arg Ser Trp Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa
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> 239
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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<220>
<221> misc_feature
<222> (79)..(83)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<220>
<221> misc_feature
<222> (85)..(89)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<220>
<221> misc_feature
<222> (134)..(138)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<220>
<221> misc_feature
<222> (140)..(144)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<220>
<221> misc_feature
<222> (231)..(235)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<220>
<221> misc_feature
<222> (237)..(241)
<223> Xaa can be any naturally occurring amino acid or any naturally
      occurring amino acid except proline or glycine

<400> 239

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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 Arg Met Glu Pro Arg
 35 40 45

Ala Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

50

55

60

Arg Lys Val Lys Ala His Ser Gln Thr His Arg Val Asp Leu Xaa Xaa
 65 70 75 80

Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa 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 Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa
 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 Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa
 225 230 235 240

Xaa 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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

260

265

270

Arg Trp Glu Pro
275

<210> 240
<211> 341
<212> PRT
<213> Homo sapiens

<400> 240

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 241

<211> 341

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<212> PRT

<213> Homo sapiens

<400> 241

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 242
<211> 275
<212> PRT
<213> Homo sapiens

<400> 242

Gly Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 243
<211> 275
<212> PRT
<213> Homo sapiens

<400> 243

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 244
<211> 275
<212> PRT
<213> Homo sapiens

<400> 244

Cys Ser His Ser Met Arg Tyr Phe Asp Thr Ala Val Ser Arg Pro Gly
1 5 10 15

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 245
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 245

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 246
<211> 275
<212> PRT
<213> Artificial sequence

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

<220>

<223> Synthetic sequence

<400> 246

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 247
<211> 276
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 247

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Arg Trp Glu Pro
275

<210> 248
<211> 276
<212> PRT
<213> Homo sapiens

<400> 248

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 249
<211> 276
<212> PRT
<213> Homo sapiens

<400> 249

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

Arg Trp Glu Pro
275

<210> 250
<211> 276
<212> PRT
<213> Homo sapiens

<400> 250

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

CUEB-110WO_SEQUENCE_LISTING_ST25.txt

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> 251
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<220>
<221> Misc_feature
<222> (2)..(5)
<223> This stretch of amino acid residues may be repeated

<400> 251

Gly Ser Ser Ser Ser
1 5

CUEB-110WO_SEQUENCE_LISTING_ST25.txt